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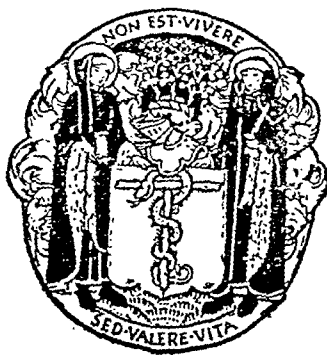
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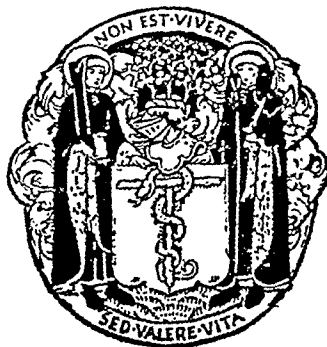
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Section of Obstetrics and Gynæcology

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[May 18, 1945]

Observations on Certain Rheological Properties of Human Cervical Secretion

By A. F. CLIFT, F.R.C.S., M.R.C.O.G.

Late Assistant, Nuffield Department of Obstetrics and Gynæcology, University of Oxford

ABSTRACT.—The object of this Communication was to demonstrate two rheological properties of cervical secretion, namely, flow-elasticity and Spinnbarkeit. There is evidence that these properties undergo cyclic variation during the menstrual cycle and bear relation to ovulation, to penetrability by spermatozoa and to pregnancy. By means of the menstroscope, designed by Scott Blair, flow-elasticity or elastic recoil can be measured. It is found to be most marked at the time of ovulation when also the mucus is thin and transparent. Spinnbarkeit—the capacity of liquids to be drawn into threads—is also capable of accurate measurement by drawing away a coverslip placed on a blob of mucus which is drawn out into a long thread. It is also more marked at the time of ovulation and is almost absent in pregnancy. Plasticity and tack, two further properties of cervical mucus, were also discussed. It is believed that these tests will prove to be of value in diagnosis of ovulation and in the study of sterility.

A study of certain rheological properties of human cervical secretion was undertaken at the suggestion of G. W. Scott Blair, D.Sc., who had observed certain significant rheological phenomena in bovine cervical secretion when working on the problems of the time of ovulation and pregnancy diagnosis in cows, at the National Institute for Research in Dairying, Reading.

Scott Blair (1937) described an emptying-tube viscometer for use with rheologically complex materials. Scott Blair, Folley, Malpress and Coppen (1941) found that the viscous and elastic properties of bovine cervical secretions vary regularly during the œstrous cycle (fig. 1). The object of this communication is to direct attention to two recently recognized rheological properties of human cervical mucus, namely, *Flow-elasticity* and *Spinnbarkeit*; and to demonstrate the *Menstroscope*, an instrument for the accurate objective measurement of *Flow-elasticity*.

There is experimental evidence which suggests that the rheological properties of human cervical mucus undergo a cyclic variation in the menstrual cycle, and bear direct relation to ovulation, to penetrability of cervical mucus by spermatozoa, and to pregnancy.

Macroscopic examination of samples of human cervical secretion show marked variations in rheological properties according to the time in the menstrual cycle at which they are collected, e.g. at mid-cycle the secretion appears translucent and fluid; at other times of the cycle samples appear more viscid; in pregnancy the mucus is characteristically thick, sticky and gelatinous.

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of force needed to draw cervical mucus into a capillary tube, and the result was qualified as low, moderate or high.

Lamar, Shettles and Delfs (1940), using this method, found that there was no relation between "relative viscosity" and penetrability. This result surprised these workers and they suggested that "viscosity" might play a much larger part in penetrability than their results indicated; admitting that any approximation of the "relative viscosity" by this method was bound to be inexact.

As recently as September 1944 it was restated that no objective method for measuring "viscosity" of cervical mucus had yet been found (Viergiver and Pommerenke, 1944).

It is now possible to make accurate objective measurements of the rheological properties of human cervical secretion.

When considering a body secretion such as cervical mucus, we must remind ourselves that secretions are not true fluids—they are complex rheological systems (*see* Note 1)—and as such they are characterized by properties such as: Anomalous viscosity—Elasticity—Flow-elasticity—Spinnbarkeit—Thixotropy—Tack—Stickiness—Adhesiveness, &c.

A study of such physical properties is called Rheology—so called to save circumlocution. Rheology is "the study of flow and deformation of matter". Many of these phenomena are imperfectly understood and undoubtedly difficult to comprehend. Conceptions based on special properties of molecules, such as polarity and length, are theoretical aids to assist in understanding them.

Efforts are being made to replace rough subjective tests by more accurate objective measurements of these rheological properties. Cervical secretion is not a truly viscous fluid, and therefore cannot be said to have a viscosity (*see* Note 3). The characteristics of a true fluid are that it flows at a steady rate under constant pressure; and that when the pressure is increased, the rate of flow increases proportionately. With cervical secretion, the rate of flow is not constant at constant pressure: it increases as the stress rises, but also decreases with increasing deformation ("work-hardening") (*see* Note 1). Secretion belongs to materials that do not give straight-line flow-curves and therefore show anomalous viscosities (*see* Note 1).

Scott Blair *et al.* (1941) concluded, after examining many samples of bovine cervical mucus (a product of secretory columnar epithelium, as in the human), using the emptying-tube viscometer, that the results were not of sufficient accuracy, and too delicate and complicated for everyday use as a means of diagnosing ovulation.

FLOW-ELASTICITY (*see* Note 2)

While carrying out these experiments, Scott Blair *et al.* (1941) observed a property hitherto unrecognized in cervical mucus—Flow-elasticity, a property which undergoes cyclic variation throughout the oestrous cycle. They designed the oestroscope, by means of which oestrus can be detected in cows by measuring elastic recoil.

It occurred to us, that since ovulation normally occurs immediately after oestrus in cows, it might well be that the phenomenon flow-elasticity is associated directly with the oestrin secretion which normally accompanies ovulation (Séguy and Vimeux, 1933, correlated an increase in urinary folliculin with visual evidence of ovulation by inspection of the ovaries at laparotomy in women). We were therefore led to investigate the possibilities of flow-elasticity of human cervical secretion, as an indication of the time of ovulation in women.

These studies have led to the development of what appears to be a simple, reliable and rapid test for ovulation in women. The measurement of flow-elasticity may also prove useful in connexion with the physiology of the passage of the spermatozoa up the cervical canal, for when the elastic recoil is greatest (which appears to be at the time of ovulation) the mucus is thin and translucent—the type of mucus in which penetrability and longevity of spermatozoa are most marked (Lamar, Shettles and Delfs, 1940). It is suggested that in addition this measurement of elastic recoil might be of use as a simple tool in endocrine studies of ovarian dysfunction.

THE MENSTROSCOPE

This instrument was designed by G. W. Scott Blair for the measurement of flow-elasticity. When a material showing flow-elasticity is caused to flow along a tube, and the pressure is suddenly released, the material recoils back, towards its original position. This phenomenon was first described by Szegvari (1924) and named by him "Fließ-elastizität", which is generally translated "flow-elasticity". Ostwald and Malss observed it experimentally (1934). Scott Blair *et al.* (1941) first observed this property in bovine secretions. These workers found that the flow-elasticity phenomenon is much less affected by contamination of the sample than is "viscosity" and is also much more easily measured.

According to Moench (1934), the degree of penetrability of cervical mucus by spermatozoa seems to depend solely on the "viscosity" of the cervical secretion. The quantity of secretion, its pH and cellular content are factors of very much less importance in penetrability.

Lamar, Shettles and Delfs (1940), working at Johns Hopkins Hospital, have shown, using their micro-tubes and barrier-marker-bubble method, that spermatozoa penetrate

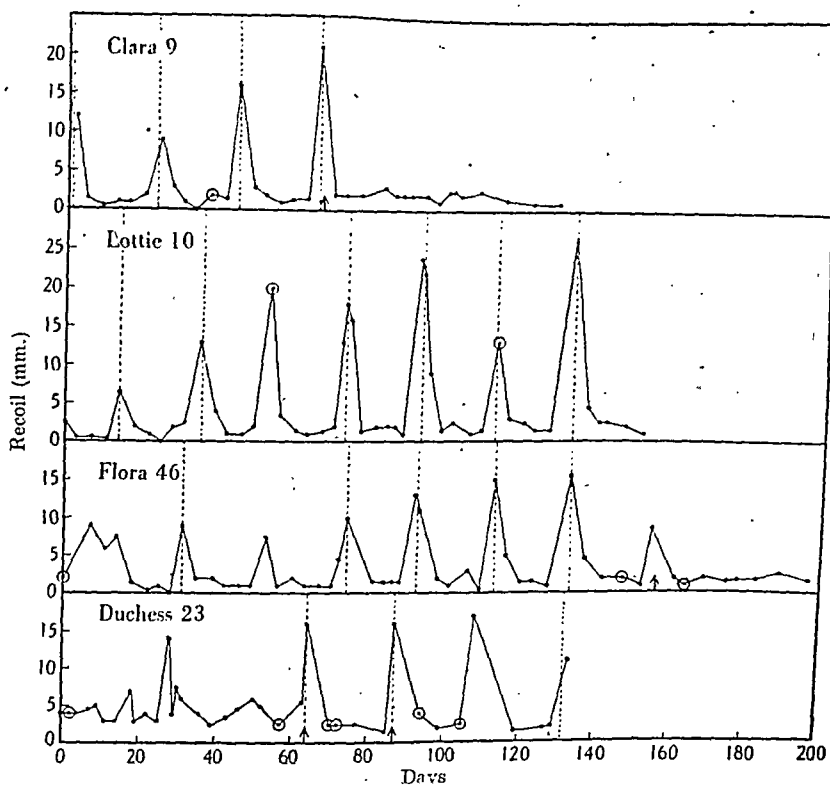


FIG. 1.—Variations in flow-elasticity of bovine cervical mucus during the oestrous cycle. Vertical broken line indicates observed oestrus and arrows denote service. Points marked with a circle are subject to a certain error due to inadequacy of sample. Clara and Flora became pregnant after the services indicated. (From *Biochem. J.*, 1941, 35, 1046. With kind permission of the Authors and the Editors of the *Biochemical Journal*.)

cervical mucus for an appreciable distance only when the mucus is translucent and thin; when the mucus is viscid (see Note 3), although the spermatozoa are strongly attracted to the mucus the viscosity impedes their upward progress—they quickly become enmeshed and devitalized.

A more analytical study of the rheological properties of cervical mucus is essential to a clearer understanding of the relation of these variations in consistency of cervical mucus to ovulation, to penetrability and to pregnancy.

"Viscosity" (see Note 3)

Robin (1848) observed the presence of "viscosity" in human cervical secretion in 1848 (many years before Sim invented his vaginal speculum). In 1925 Woodman and Hammond gave a detailed description of the variations in the physical properties of bovine cervical secretion during the oestrous cycle and pregnancy in cows.

Many workers on cervical mucus have realized the importance of "viscosity" in human cervical secretion in relation to ovulation and penetrability (Kurczok and Miller, 1928; Séguy and Vimeux, 1933; Séguy and Simmonet, 1933; Moench, 1934; Lamar, Shettles and Delfs, 1940; Viergiver and Pommerenke, 1944) but, until recently, no one has been able to measure accurately the "viscosity" of cervical secretion.

In the past "viscosity" was subjectively estimated roughly as thin or thick. Later, an attempt to measure "relative viscosity" (see Note 1) was made by estimating the amount

translucent and fluid—both are characterized by Spinnbarkeit and flow-elasticity—and both readily form tough bubbles on homogenization. In white of egg, Spinnbarkeit is more marked, elastic recoil less marked, than in mid-cycle cervical secretion.

One concludes that the molecular construction may well be somewhat similar in both materials. Penetrability of cervical mucus by spermatozoa probably depends on the molecular arrangement of the cervical secretion.

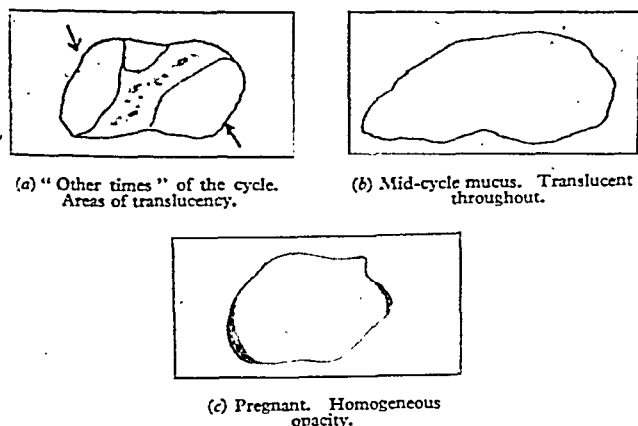


FIG. 4.—Diagrammatic representation of the macroscopic appearance of various samples of human cervical mucus (a, b, c).

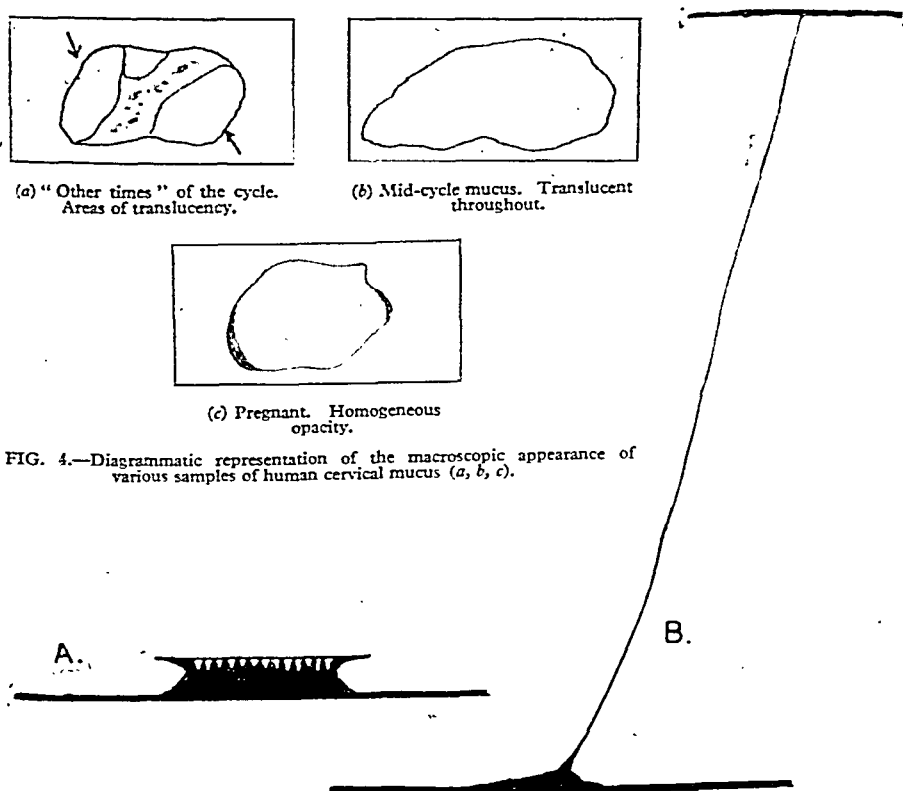


FIG. 3.—Diagrammatic representation of Tack and Spinnbarkeit. A, Tack (as seen in pregnancy cervical mucus); B, Spinnbarkeit (as seen in mid-cycle cervical mucus).

It is reported that artificial insemination with semen mixed with white of egg is a more successful procedure (about 5%) than artificial insemination with semen alone (under 1%). Considering that thin and translucent cervical mucus, giving peak elastic recoil and maximum Spinnbarkeit (as is present at the time of ovulation), provides the optimum conditions for the height of penetrability of spermatozoa—and considering the therapeutic value of fresh white of egg in artificial insemination—it would be logical to suggest that a sample of cervical mucus with the above characteristics, obtained from a fecund donor at the time of ovulation, should be used together with semen for artificial insemination, i.e. to consider the soil (cervical mucus) as well as the seed (spermatozoa) in artificial insemination. Such a procedure is suggested in view of the disappointing results of artificial insemination with semen alone.

PLASTICITY

Plasticity is that property which enables a material to be deformed continuously and permanently without rupture, during the application of a force that exceeds the yield-value of the material.¹

Plasticity is a characteristic of pregnant cervical mucus.

A rheological law as applied to cervical mucus can be laid down as follows: "Plasticity predominates in pregnancy—Elasticity in non-pregnancy, especially at ovulation time."

¹ The yield-value is the pressure below which the material does not yield appreciably.

The menstroscope consists essentially of a graduated glass capillary tube of about 0.75 mm. bore, 10 cm. long and graduated in mm., with the glass drawn down to 3 mm. bore. One end fits on to a 2 c.c. Record syringe and a small side-tube 3 mm. bore is interposed between the tube and the syringe.

The test is carried out as follows: A dry sterile speculum is inserted into the vagina and a sample of cervical mucus is collected with a pair of long artery forceps—at mid-cycle a generous sample can usually be collected; at other times of the cycle, when the amount of mucus may be scanty, further secretion can be aspirated through a long glass pipette.

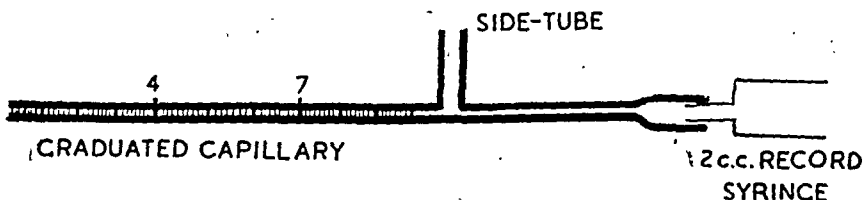


FIG. 2.—The menstroscope, for measuring flow-elasticity.

The collected sample of mucus is roughly homogenized by squeezing between two glass slides, one of the glass slides can be conveniently used for manipulating the blob of mucus. With the side-tube closed with a finger, mucus is drawn into the capillary tube until the meniscus reaches the 7 cm. mark. Keeping the side-tube closed, and the apparatus horizontal, the column of mucus is then slowly forced out of the capillary until the meniscus reaches the 4 cm. mark. At this point the finger is quickly removed from the side-tube, thus suddenly releasing the pressure on the column of mucus, the flow-elasticity of which causes the meniscus to recoil along the capillary. The amount of recoil in mm. is noted.

The menstroscope is made by Vann Bros. Ltd., and is made in perspex; the advantages over glass are that it is boilable and unbreakable in all normal conditions—the disadvantage is that care has to be taken which disinfectants are used, since some of them attack perspex.

In performing the elastic recoil test the following points should be strictly observed:

- (1) The cervix must be *healthy*—there must be no pathological tear, no marked erosion or endocervicitis.
- (2) Contamination with blood should be reduced to a minimum.
- (3) The specimen must be collected from the cervical canal—not from the vaginal vault or external cervical os.
- (4) Neither douching nor coitus must have taken place during the forty-eight hours preceding collection.
- (5) No antiseptics must be used in collecting the sample—only dry sterile instruments are used.
- (6) The elastic recoil test should be performed within twenty minutes of collection of the sample.

SPINNBARKEIT (Fibrosity)¹

This is the capacity of liquids to be drawn into threads. White of egg shows this property to a marked degree. Erbring (1936) studied Spinnbarkeit in detail; he takes a narrow capillary tube, with a conical mouth into which he sucks the material—he then withdraws the tube at a constant rate and measures the maximum length of the fibre which can be produced before rupture occurs. Over a considerable range, the length of the thread which can be drawn is generally proportional to the speed of drawing, which therefore should be kept as constant as possible. Erbring (1936) finds that there is no universal connexion between the maximum length of the fibre under standard conditions, and either viscosity or surface tension. Spinnbarkeit, capable of accurate objective measurement, is a property of cervical mucus, but it is present only to a marked degree when flow-elasticity is at its height, i.e. in mid-cycle samples. It appears to be directly related to ovulation and to the type of mucus in which penetrability by spermatozoa is greatest. Spinnbarkeit is only seen to a much less degree at other times of the menstrual cycle, and is more or less absent in pregnancy.

The test is carried out by drawing away a coverslip placed on a blob of mucus—the mucus is drawn into a long thread. At present we are estimating Spinnbarkeit by measuring the length of the thread in cm. The construction of an instrument for accurate objective measurement (such as that used by Erbring) is under consideration.

It is an interesting observation to note the marked similarity of the rheological properties of mid-cycle cervical secretion and fresh white of egg. Both these substances appear

¹ Rheologists are at present discussing a more suitable English term for this property.

The number of leucocytes was determined by microscopic examination.

Recoil values determined in samples from three subjects at intervals over a period covering 3, 2, 2, menstrual cycles respectively are shown plotted in fig. 5.

It is clear that the flow-elasticity of the cervical mucus varies regularly during the menstrual cycle, rising to a maximum about the time of ovulation. It is desirable to investigate the way in which the elastic recoil values vary day by day during the mid-cycle. Facilities for such an experiment have unfortunately not yet been available but it is hoped that this may be done in the near future.

Two of the women became pregnant during observation, the periodicity in elastic recoil immediately disappeared and the values remained at a low level.

The periodicity in the flow-elasticity of the cervical mucus, correlated with the time of the mid-cycle, appeared to afford a basis for an objective method of diagnosis of ovulation, particularly as this property can be measured so rapidly and easily. Since failure of ovulation is one of the causes of functional sterility, there is need of a simple, yet reliable method for the detection of ovulation. In order, therefore, to investigate the

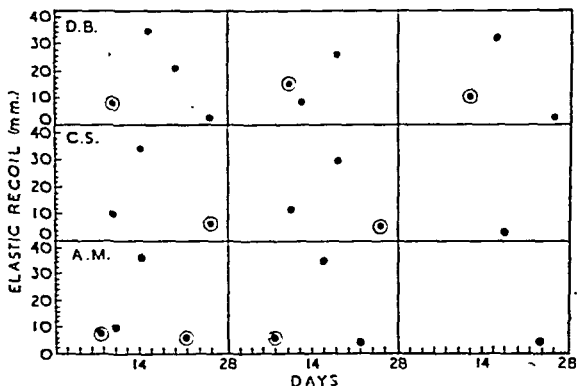


FIG. 5.—Variations in flow-elasticity of human cervical mucus during the menstrual cycle and in pregnancy. Points marked with a circle are subject to a certain error due to inadequacy of sample. C. S. and A. M. were subsequently proved to be pregnant.

value of flow-elasticity measurements as a practical method for the diagnosis of ovulation, numerous determinations have been made on samples from women in various phases of the menstrual cycle.

Fig. 6 summarizes the results of tests on 26 women.

Comparing the figures it is clear that the elastic recoil values for samples taken about the time of ovulation are significantly higher than for samples taken at other times of the cycle or in pregnancy. On the basis of our data, therefore, it may be concluded

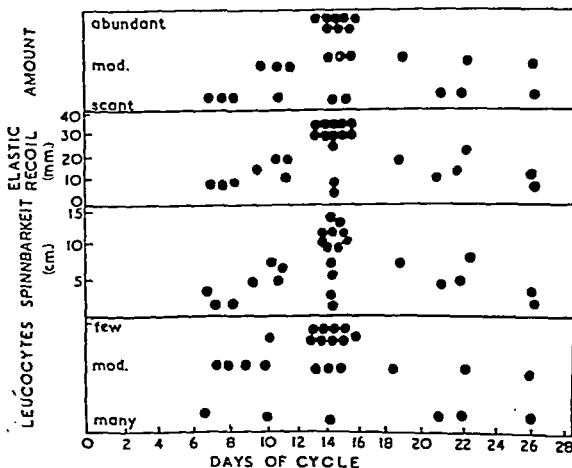


FIG. 6.—Relation between the amount of cervical mucus, its elastic recoil, Spinnbarkeit, number of leucocytes contained and the time in the menstrual cycle. These curves are based on observations on 26 women with normal menstrual cycles.

TACK

Tack (a form of stickiness) is another independent property of cervical mucus, but is only seen to a marked degree in pregnant samples. All samples of cervical mucus show stickiness to some degree, but tack is a particular form of stickiness.

In practice, tack is measured by quickly drawing away a coverslip from a blob of mucus placed on a glass slide. The mucus does not form into long threads, but the whole surface of the blob adheres to the coverslip and can be drawn only a slight distance away from the glass slide—about a cm. or two.

A more exact measurement can be made of this property by a specially contrived apparatus ("The Tackmeter", see Green, 1941).

Examination of the sample under the microscope after performing the test shows a tree-like pattern.

OBSERVATIONS ON 143 COLLECTED SAMPLES OF HUMAN CERVICAL SECRETION,
NON-PREGNANT AND PREGNANT

A. Mid-cycle Samples (11 of 13 Samples).

Quantity: Abundant.

Appearance: Translucent throughout, optically clear—very glassy.

Consistency: "Runny" (not cohesive or tacky).

Cellular content: Scarcity of cells, and these cells show a movement (not Brownian) due to the viscosity of the fluid.

Tough bubbles form very readily when homogenizing the secretion between two glass slides—these bubbles are difficult to break up.

Spinnbarkeit: Very marked—mucus can be drawn into very long threads 10 to 13 cm. long.

Elastic recoil: Very marked—av. 30 mm. and recoil is "lightning" in speed.

All the above properties were present to a marked degree in 11 samples collected at the mid-cycle. These properties were more or less absent in samples collected at other times of the cycle—and in pregnancy.

B. Post-menstrual Samples.

Quantity: Moderate.

Appearance: Translucent areas, with only tiny specks of opacity (i.e. not homogeneously opaque).

Consistency: Not as "runny"—more cohesive than at mid-cycle, but not tacky or but slightly so.

Cellular content: Moderate—no cell movement seen.

Tough bubbles: Do not form on homogenization.

Spinnbarkeit: Not present—or but slightly so (1 cm.).

Elastic recoil: Av. 10 mm.

C. Premenstrual Samples.

Quantity: Scanty.

Appearance: Translucent areas with small areas of opacity (not homogeneously opaque).

Consistency: Not as "runny"—more cohesive than at mid-cycle. Not tacky or but slightly so.

Cellular content: Moderate to abundant—no movement seen.

Tough bubbles: Do not form on homogenization.

Spinnbarkeit: Not present or but slightly so.

Elastic recoil: Av. 8 mm.

D. Pregnant Samples.

Appearance: As early as the 6th to 7th week of pregnancy (seven samples) the secretion shows a characteristic homogeneous light opacity—i.e. it loses its translucency throughout. Later in pregnancy this opacity becomes more pronounced.

Consistency: Cohesive—one piece—it tends to hold together. It is thick and sticky (not "runny") and shows characteristic tackiness.

Cellular content: Very abundant, no movement seen.

Tough bubbles: Do not form on homogenization.

Spinnbarkeit: Is absent or only slightly present.

Elastic recoil: 6th to 7th week to 10th week, value may be up to 6 mm. and recoil is slow.

After 10th week the mucus is difficult to draw into the menstroscope—recoil is absent.

RESULTS

Our results, at first, made no sense whatsoever. It was only after some months of work, that we realized how important it was to deal only with samples collected from the healthy cervix, in order to study first principles.

In all, the cervical mucus of 26 women showing normal cycles has been studied. Seven of these individuals have been seen more than once and 3 studied for at least one cycle.

An attempt was made to correlate the amount of mucus secreted, macroscopic appearance, elastic recoil, Spinnbarkeit and the number of leucocytes contained.

Mucus was judged to be (1) scant, (2) moderate, (3) abundant, at the time of collection.

Elastic recoil was determined by the menstroscope, Spinnbarkeit was measured in cm.

that the elastic recoil value of 25 mm. and upwards means that when the sample was taken, the woman concerned was about the time of ovulation.

A feasible explanation of the marked rheological changes in cervical mucus about the time of ovulation is that they are brought about by the direct action of the ovary through folliculin in the blood-stream, on the cervical mucus. It is known that follicular fluid dissolves cervical mucus. (It is of interest to note that Rowlands and MacLean were unable to show that hyaluronidase of semen dissolves the mucoprotein of cervical secretion.)

These observations are presented because they may point the way for further investigation.

SUMMARY

(1) "Viscosity" of human cervical secretion is discussed. Cervical mucus is not a truly viscous fluid and cannot be said to have a viscosity. Its changing "viscosity" (anomalous viscous behaviour) with varying stress and strain can be effectively measured in a Scott Blair emptying-tube viscometer, but the apparatus is too delicate and complicated to be of practical everyday use as a test for ovulation or pregnancy.

(2) Rheological properties—*Flow-elasticity* and *Spinnbarkeit*—hitherto unrecognized in human cervical secretion, are described. Both phenomena occur to a marked degree only in mid-cycle samples, and therefore form the basis for a rheological test for ovulation in woman. These properties are maximum only in "thin and translucent" samples, i.e. when penetrability and longevity of spermatozoa are greatest. These phenomena are absent in pregnancy samples.

(3) Means of accurate objective measurement of flow-elasticity (*the menstroscope*) and *Spinnbarkeit* are described. These methods are simple and rapid and more reliable than methods used to estimate "viscosity" and "relative viscosity".

(4) A rheological test for ovulation in woman is described—namely the sample of cervical mucus is "runny"; homogeneously translucent; elastic recoil and *Spinnbarkeit* are maximum; tough bubbles, which are difficult to break up, readily form on homogenizing the sample; cellular content is minimal, and these few cells show movement typical of mid-cycle samples.

(5) Considering the molecular construction of cervical mucus, it is suggested that the addition of donated cervical mucus (characterized by maximum elastic recoil and *Spinnbarkeit*) to semen, might be used with advantage in artificial insemination of cases of cervical hostility (absence of suitable cervical secretion).

(6) Tack is described—a property characteristic of pregnancy cervical mucus.

(7) A rheological test for pregnancy in woman is described—namely, the sample of cervical mucus is thick (not "runny"); homogeneously opaque; the mucus is difficult to draw into the menstroscope; there is more or less absence of elastic recoil and *Spinnbarkeit*; tough bubbles do not form on homogenizing the sample; and tack is characteristically present (the above description applies to samples as early as the seventh week of pregnancy).

(8) It is believed that the described rheological phenomena and tests should prove of practical value in the recognition of ovulation and anovulatory cycles; in the investigation and treatment of cases of cervical hostility; as a useful tool in endocrinology of ovarian dysfunction; and as accessory tests for pregnancy.

This work was carried out in the Nuffield department of Obstetrics and Gynaecology under Professor Chassar Moir, to whom I wish to express my appreciation for help and encouragement, and I wish particularly to thank G. W. Scott Blair, D.Sc., rheologist, for freely giving of his time and valuable scientific knowledge. I would stress that this investigation forms an admirable example of the need for co-operation between workers trained in different fields. Results would have been meagre without the co-operation of trained rheologists and medical personnel. I am also grateful to Mr. John Stallworthy, Mr. Scott Russell, Dr. Fynn and Dr. Dorothy Newell for providing mucus samples from patients.

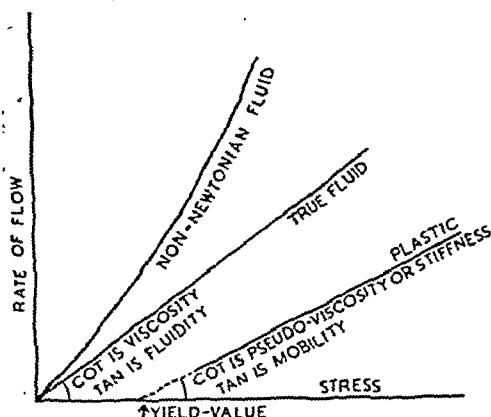
NOTES BY G. W. SCOTT BLAIR, D.Sc.

NOTE 1.—Anomalous viscous behaviour is the general term for any "runny" material that is not a true fluid. There are many kinds of anomaly, the principal types being:

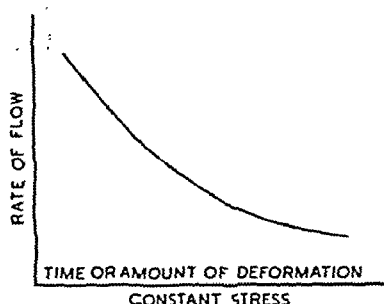
(a) Non-Newtonian fluids ("Pseudo-plastic" has almost the same meaning).—These start to flow at the smallest pressures, i.e. have no yield-value and are therefore not "plastic". The rate of flow is not proportional to pressure but increases either more or less rapidly than would a true fluid. The former case is the commoner (see Graph 1).

A complicating factor is that in practice, such curves cannot be directly obtained for spinnbar materials because the ratio of pressure (stress) to rate of flow not only falls with rising stress but increases with increasing deformation (work-hardening). This is very important. Hence we have Graph 2.

(b) Plastic behaviour.—Up to a certain stress (the yield-value) there is no flow. Above this flow is often proportional to the (stress minus yield-value), i.e. the line is straight. (The bottom part is usually anomalous and is therefore dotted in. The yield-value is generally got by extending the experimental straight line to the stress axis, but there are other yield-values defined in other ways) (see Graph 1).



Graph 1.—To illustrate the meaning of certain rheological terms.



Graph 2.—To illustrate a type of work-hardening.

Mobility is defined as $\frac{\text{rate of flow}}{(\text{stress minus yield-value})}$ and should be used only to mean this. Its reciprocal, $\frac{(\text{stress minus yield-value})}{\text{rate of flow}}$ is called "stiffness" or "pseudo-viscosity". The reciprocal

of viscosity (of a true fluid) (i.e. $\frac{\text{rate of flow}}{\text{stress}}$) is called "fluidity". These terms should only be used in the strict sense. English rheologists (not American) still use "consistency" as a general term for "general viscosity".

Relative viscosity (of a true fluid) simply means the number of times a liquid is more viscous than water, e.g. an oil has a viscosity at 25° C. of 50 centipoises. Water at 25° is almost exactly 1 c.p., hence "relative viscosity" of oil is "50".

Note 2.—Flow elasticity is usually paralleled by the onset of Spinnbarkeit, a reduced consistency and perhaps a fall in nitrogen content.

Note 3.—The use of "viscosity" (or "fluidity") in anomalous systems.—Some rheologists agree to speak of a viscosity defined for arbitrary stress-strain conditions but all are agreed that "the viscosity" has no meaning. The Americans tend to use "consistency" to mean "a viscosity" but this use is not popular in England. The term "viscid" has no special sense for rheologists.

Professor Chassar Moir assured members that the changes in the cervical secretion—some of which could be so clearly and easily demonstrated by the "menstroscope"—were of a very real nature.

Dr. G. W. Scott Blair: Those unfamiliar with rheology are apt to be rather overwhelmed by the abundance of rheological properties. In fact, it is all to the good that most biological "fluids" are not "true fluids", i.e. do not flow at a constant rate under steady pressure, the rate being proportional to the applied pressure. "True fluids" would only give us one flow property (viscosity) to correlate with the factors we wish to study. As it is, there are many factors which can be correlated; but it is naturally important that they should be clearly distinguished and adequately measured.

The measurement of flow-elasticity (or Spinnbarkeit which is often associated with it) has given us a good practical test for oestrus in the cow and a study of more complex rheological properties of cervical secretions an interesting, though not yet reliable, correlation with bovine pregnancy.

Through the skill and perseverance of Mr. Cliff it now seems likely that similar methods may be of use in detecting ovulation and pregnancy in the human.

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Some New Facts Concerning the Prognosis and Treatment of Carcinoma of Cervix by Radiation

By MALCOLM DONALDSON, F.R.C.S., F.R.C.O.G.

In 1922 the late Dr. Canti and I were interested in the problem of how radium brought about the destruction of cancer cells in carcinoma of the cervix. We cut sections before and after treatment and discovered some obvious changes [1], but did not get very far in the solution of the problem. At that time, the late Dr. Strangeways was doing some of the earliest *quantitative* work on the biological effects produced by X-ray. He used fibroblasts in tissue culture. We then joined forces [4] and Strangeways and his collaborators did some pioneer work on the subject [2]. This type of work has continued at the Strangeways Research Laboratories ever since, and recently Dr. Spear and Dr. Glücksmann started their systematic work on the effects of irradiation on tissue *in vivo* and have now shown that similar quantitative methods are applicable to growth under these conditions.

I do not propose to trace all the stages of their investigations which eventually brought them to their work on human malignant tumours [3, 5].

In treating carcinoma of the cervix by radiotherapy for many years, certain puzzling questions arose, why, for example, among Stage 1 cases should only 50% do well and the other 50% do badly? Again, the majority of advanced cases ended fatally within a few months and the growth did not clear up even close to the radium applicator, although it was obvious that the malignant cells locally got as much irradiation as the cells in the early and successfully treated cases. It is also true that occasionally an advanced case which had been given a small dose, possibly as a placebo, cleared up and lived for years.

It was easy to say that some growths are more radio-sensitive than others, but that did not help to advance the subject. I think it is fair to say that Spear and Glücksmann are the first to throw any real light on this very important subject of radio-sensitivity.

The first point that they have proved is that with the "Stockholm Technique" and its modifications the most "radio-curable" are the *well-differentiated growths* and not the *undifferentiated growths*. I use the word radio-curable to mean the disappearance of carcinoma cells in sections taken after treatment. This came as a surprise to some of us who had observed large hypertrophic growths (which were assumed to be undifferentiated) disappear macroscopically in a few weeks. Some of these tumours in fact are differentiated, some undifferentiated, and it has now been found that it is the anaplastic type of growth which on section more frequently shows a persistence of viable malignant cells after irradiation.

It is important to be quite clear as to what we mean by the terms Differentiated and Undifferentiated growths. In "Differentiated" growths, which we will call Anaplastic Squamous (AS), the cells when young resemble normal basal cells, but when growing old they either undergo normal keratinization giving rise to typical cell nests or they undergo abnormal keratinization giving rise to an aggregation of basal cells round a necrotic core (fig. 1).

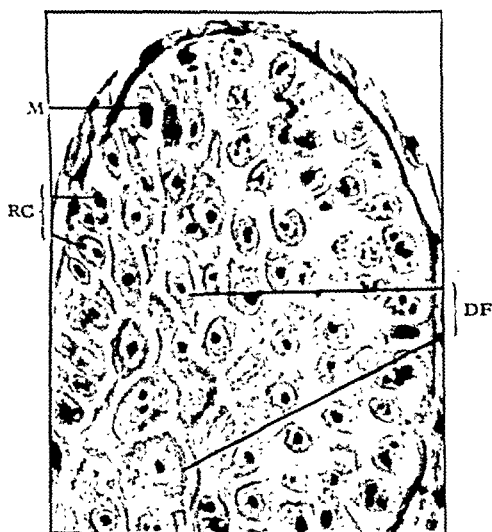
In "Undifferentiated" tumours called Anaplastic Parakeratotic (AP), the cells when young are capable of active mitosis, but degenerate as they get older by a process of cytoplasmic condensation (parakeratosis) or by nuclear disintegration (fig. 2).

If a large number of differentiated and undifferentiated tumours are classified according to the stage of the disease, when first seen it will be found that the differentiated tumours predominate in the early stages, and the undifferentiated tumours in the late stages.

TABLE I.—STAGE DISTRIBUTION AMONG TUMOUR TYPES.

	Differentiated (AS type)	Undifferentiated (AP type)	Columnar cell tumours
Stage 1 ...	50%	44%	6%
" 2 ...	34%	62%	4%
" 3 ...	23%	71%	6%
" 4 ...	12%	82%	6%

Why are there more differentiated growths in Stages 1 and 2 than in Stages 3 and 4? It is tempting to suggest that a well-differentiated growth if left untreated becomes an un-

FIG. 1. $\times 550$.

RC = resting cell. DF = differentiating cell.
M = mitotic cell.

Shows some young undifferentiated cells with small amount of cytoplasm, darkly stained nuclei, and absence of distinct cell wall. The section also contains some more mature cells which show differentiation and the nuclei are paler, the cytoplasm is eosinophilic and there is a clearly defined cell wall.

FIG. 2. $\times 550$.

Resting (RC) and mitotic cells (M) only. Shows cells which all have dark nuclei, and there are no cells showing typical differentiation.

FIG. 2.—The four cell types:

RC = resting cells } viable.
M = mitotic cells }
DF = differentiating cells } non-viable.
DG = degenerating cells }

FIG. 3. $\times 700$.

differentiated growth. If this were so, it would be expected that there would be a longer history in undifferentiated growths than in differentiated growths in the same stage.

It is impossible to get an accurate history of duration of the disease, but judging from the length of time irregular bleeding has continued there is no evidence of any difference in the *average* duration of symptoms between the two types of tumour in the same stage though a few growths give quite long histories. It is also interesting to note that the average history of Stage 1 and Stage 4 is 4.2 months and 7.5 months respectively. It seems, therefore, that a tumour staged as 4 is more often one which has grown quickly than one which has been slowly growing for a long time, but it still remains to be explained why a quickly growing tumour does not give rise to symptoms in the early stages and thus attract attention.

Glücksmann has studied pre-radiation sections of 346 tumours in which a five-years' follow-up was possible, and found that of the 87 differentiated tumours 28 patients lived for five years or more = 32%, but of the 259 undifferentiated tumours only 40 lived for five years = 15%.

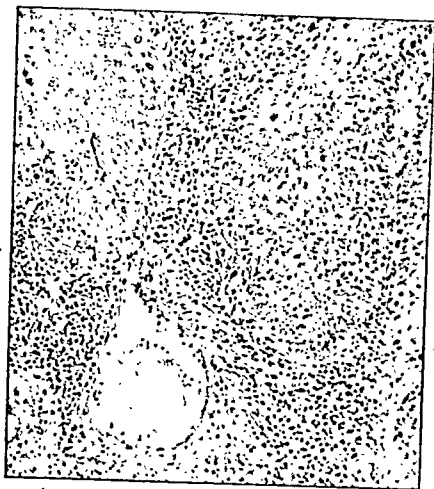


FIG. 4.—Day 0: pre-radiation biopsy showing a young area. $\times 175$.

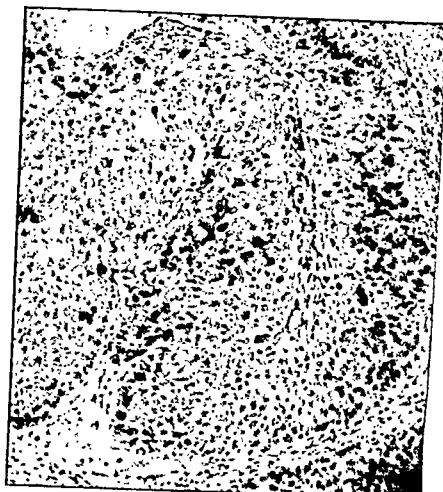


FIG. 5.—Day 13: biopsy after two irradiations (no change). $\times 175$.



FIG. 6.—Day 35: biopsy after three irradiations (no change). $\times 175$.



FIG. 7.—Day 179: biopsy is practically indistinguishable from the pre-radiation specimen when the young areas are examined. $\times 175$.

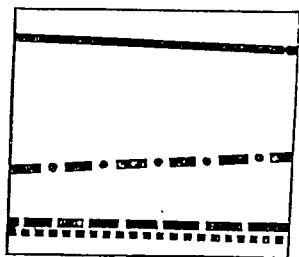


FIG. 8.—Quantitative histological chart of counts from AP tumour shown in figs. 4 to 7.

— Resting cells.
 - - - Differentiating cells.
 . . . Degenerating cells.
 - . . Mitotic cells.

There are only minor variations in the cell counts throughout the period of observation. Death occurred at month 7. Clinically this was considered at first unfavourable, then as doing well, but finally as unfavourable.

FIG. 8.

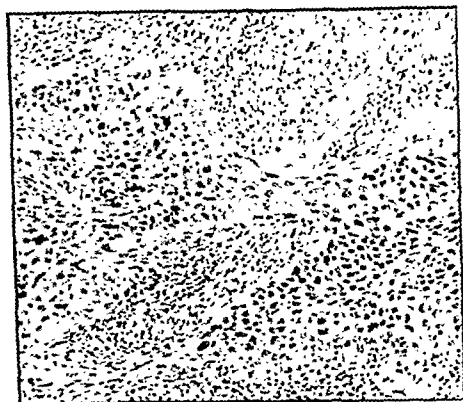


FIG. 9.—Day 0: pre-radiation biopsy showing a young area of growth. $\times 95$.

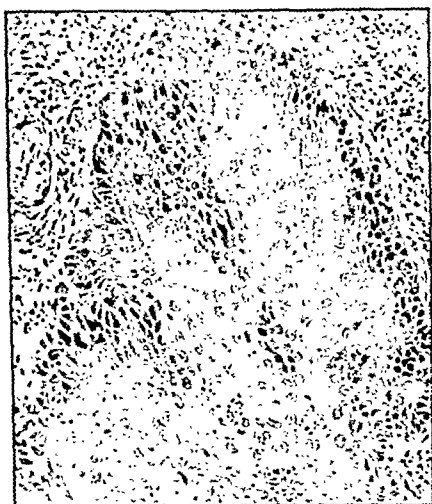


FIG. 10.—Day 2: marked increase in cell size and in the number of differentiating cells. $\times 95$.



FIG. 11.—Day 7: further increase in cell size; reduction in the number of resting cells. $\times 95$.



FIG. 12.—Day 11: only non-viable malignant cells left. $\times 95$.

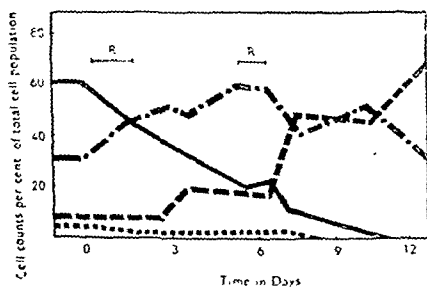


FIG. 13.—Quantitative histological chart of case shown in figs. 9 to 12. There is a rapid fall in the numbers of viable cells (i.e. resting and mitotic) and a rise in the numbers of non-viable cells (i.e. differentiating and degenerating) up to Day 6. Then differentiating cells begin to break down and degenerate (— line falls and - - - line rises). [From *Brit. J. Radiol.*, 1941, 14, 192.]

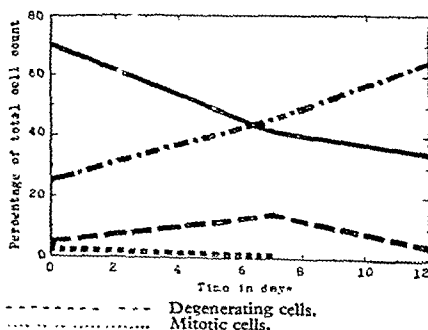


FIG. 14.—An AP type tumour, clinical Stage 3, seventy-two-hour treatment, showing slow but favourable type of response to treatment at biopsy site.

TABLE II.—THE FIVE-YEAR SURVIVAL RATES FOR 346 PATIENTS WITH TUMOURS OF THE AP OR AS TYPE.

Clinical stage	AP tumours			AS tumours		
	No. of cases	Five-year survivors		No. of cases	Five-year survivors	
1 ...	15	6	40%	15	7	46%
2 ...	48	11	23%	27	9	33%
3 ...	107	18	16%	32	11	34%
4 ...	80	5	5%	13	1	7%
Totals	250	40	15%	87	28	32%

The table shows quite clearly that tumours of the AP type respond less well to radiation treatment (by the technique here used) than those of the AS type, the difference being most marked in clinical Stage 3, where the proportion of patients with AS tumours who survive five years is more than twice the corresponding figure for patients with AP tumours.

At first sight it might be thought that the greater number of well-differentiated tumours in Stages 1 and 2 would account for the better results in well-differentiated tumours, but a glance at Table II shows that in the same stage the well-differentiated do better than the undifferentiated. Further it might be thought that the patients with AP tumours in Stage 3 did badly because these growths had already given rise to metastases. This may be true in some cases but the fact that sections taken from the primary growth after treatment still show growth to be present, and that the recurrence occurs *within* the irradiated area proves that there must be a difference in the reaction of these tumours to irradiation compared with the AS tumours.

In addition to being able to state whether a tumour is likely to be "radio-curable" (i.e. that the tumour is not likely to recur in the treated area) by a study of the pre-radiation biopsy, Glücksmann has worked out a method whereby it is possible to make a more accurate prognosis of the final results of the treatment on the local growth in any given case. *This is done by a quantitative study of post-radiation sections for comparison with the pre-radiation section.* This method has been worked out on sections taken from many institutions, and among these is Mount Vernon Hospital. I send sections to Dr. Glücksmann at Cambridge who works out the prognosis, and I go up about once a quarter with the clinical notes of the case to compare the results.

The following is the method by which the tumour response is judged.

Sections are always taken from the growing edge of the tumour. This is an important point, as, if sections are taken from the centre of the growth, the cells may be too necrotic to give results of any value. I may add that Dr. Glücksmann has taken many sections from the growing edge of different parts of the same tumour, where a cancer has been excised, and the slides have shown the same picture in each selected portion of the tumour.

Having obtained a pre-radiation section, percentage counts are made of the following four types of cells:

A. *Resting cells.*—These are stock cells which are not differentiating and not dividing, but which retain the power to divide (fig. 2).

B. *Mitotic cells.*—These need no definition. A cell is counted as a dividing cell whatever the stage of mitosis.

C. *Differentiating cells.*—These are recognized by an alteration in the structure of the cytoplasm, which becomes eosinophilic and there is a distinct cell wall. This alteration may proceed to parakeratosis or to true keratinization. Either process renders the cell non-viable (fig. 1).

D. *Degenerating cells.*—These are moribund cells showing various forms of nuclear disintegration (fig. 3).

Biopsies are then taken on at least two occasions after the treatment has begun and the percentage counts made in the same way. All the counts are then plotted on a graph against time on a convenient scale.

Two series of micrographs will illustrate the method in practice. The first series shows histological appearance of serial biopsies from an unsuccessfully treated tumour (figs. 4, 5, 6, 7). Fig. 8 shows a quantitative histological chart made from counts in the above examples.

The second series illustrates a successfully irradiated tumour (figs. 9, 10, 11, 12).

Fig. 13 shows a quantitative histological chart made from counts in figs. 9-12.

It is now necessary to see how the prognosis given by the histologist within three weeks of the treatment, and which depends on the reaction of the primary growth as revealed by these cell counts, agrees with the prognosis given by the clinician who sees the patient from time to time in the "follow-up". In many cases the clinician is too optimistic in the early months, as he sees the growth disappear macroscopically, but after two years the difference between the two prognoses has disappeared in most cases as will be seen in Table III.

TABLE III.—COMPARISON OF HISTOLOGICAL* AND CLINICAL EVALUATION OF TREATMENT RESULTS AT INTERVALS IN A SERIES OF 150 CASES OF UTERINE CARCINOMA.

		1-4	5-8	Months 9-12	13-24	Over 24
Agreements (in number of cases)		82	104	108	111	111
Disagreements	" "	68	42	30	38	25†
No report	" "	0	4	3	1	14‡

* The histological evaluation is made within three weeks of beginning treatment.

† Includes 9 patients known to have had insufficient treatment in affected regions at a distance from the biopsy site.

‡ Among the "14 no reports" for "over 2 years" column are a number of patients not yet two years from treatment.

If, as I believe, this method is of value in giving a prognosis, then we should be able to use such curves in judging between the effect of different techniques without waiting for five years in order to compare the results of such methods of treatment. Realizing that the undifferentiated cases do badly, I decided to try a modified technique, and have now as a beginning treated 38 cases using the same amount of radium, the same number of hours, but a continuous dose instead of interrupted applications. It is too early to make any statement as to the clinical results but the histological picture suggests a definite improvement.

So far I have tried to point out the importance of the histology in making a prognosis in case of carcinoma of the cervix treated by irradiation, and the value of such observations in planning new techniques. This does not explain all our failures, there are many other factors which must be investigated and one important factor is the distribution of the irradiation. The ideal to be aimed at is an equal distribution of irradiation over the whole area affected by the growth. Dr. Neary has studied this problem very carefully and in 1943 published a paper in the *British Journal of Radiology*, 16, 225-233, and has constructed an applicator embodying these ideas. An applicator embodying some of these principles has also been designed by Mr. Blomfield with the vaginal radium in the middle line. I do not think that his design will give a good distribution of the radiation although it will be more adaptable to different-sized vaginae.

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Dr. G. J. Neary stated that he had shown in his paper that the radium in the uterus should be concentrated as far as possible near the fundus and that the radium in the vagina should be placed at the mid-line. Further, the amount of this vaginal radium should be very considerably increased in order to produce an appreciable improvement in the dose at the more outlying region of spread of the disease in the pelvis. The increased amount of radium in the vagina necessitates the use of heavy absorbing screens of platinum or similar metals in order to protect structures such as the rectum from excessive irradiation.

An applicator embodying these principles has now been constructed (with the aid of a grant from the Medical Research Council) to Dr. Neary's design and the work was executed by Mr. Powell and Mr. Aldridge of Messrs. Johnson, Matthey & Co. Ltd. It must be emphasized that there is a wide latitude in the actual design decided on. The applicator referred to here is only one possible version and is intended as an experiment and, if successful, a range of applicators of different sizes will be used. It is in three sections; the uterine tube of adjustable length contains 70 mg. of radium and is inserted first. Next the upper half of the vaginal portion is inserted, followed by the lower half. The whole system is then simply locked together whereupon the vaginal radium consisting of two sources of 140 mg. each is inserted. The total treatment time is to be about 72 hours. The transverse diameter of the vaginal portion of the applicator is 4 cm., the antero-posterior diameter 3½ cm. The diameter of the uterine tube is 7 mm., the length may be adjusted between 3.3 and 5.3 cm.

The dose around the internal os and parametria is 7,000 to 8,000 r (fig. 1). The maximum dose at the pelvic wall (fig. 1) is 5,400 r while the average dose over a 5 cm. length of the pelvic wall around B is 4,700 r. The average dose to the posterior vaginal wall is

about 4,500 r (rectum, not more than 4,000 r). Figs. 1 and 2 show a comparison of the dosage with that in the average Marie Curie technique, deduced from the data of Mayneord and Honeybourne (*American Journal Roentgenology and Radium Therapy*, 45, 235-249, 1941). This shows a transverse section across the pelvis at the level of the internal os. The very much improved lateral extension of the radiation field of the new applicator is clear, the pelvic wall dose being 5,400 r instead of 2,000 r in the Marie Curie technique.

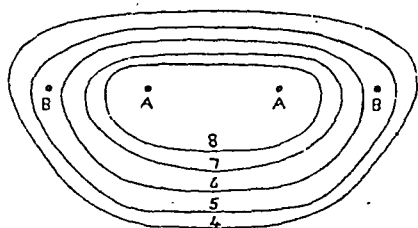


FIG. 1.

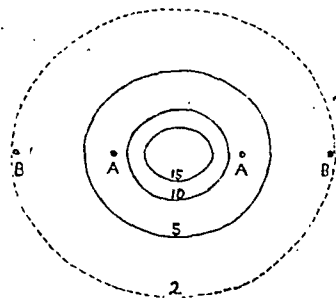


FIG. 2.

Dosage in transverse section through pelvis at level of internal os, viewed from front.
FIG. 1: New applicator. FIG. 2: Marie Curie technique. Numbers refer to thousands of r units.
(A) (parametrium) is 2 cm. from mid-line; (B) (pelvic wall) is 5 cm. from mid-line.

The applicator is fixed and supported in position by a strong harness attached by straps and belt to the patient. (*Brit. J. Radiol.*, 1943, 16, 225.)

Mr. Anthony Green: In certain cases of carcinoma of the cervix the main point is the increased dose obtained in the outer part of the broad ligament, and Neary's appliance is an important advance. The disadvantages of the applicator would appear to be first, that 70 mg. of radium is concentrated against a very small section of the interior of the uterus, thus raising the dosage in r units to a level much greater than has ever been done before. It is possible that this may be dangerous, and produce local uterine radionecrosis. Only the results can show whether this is produced or not. A second disadvantage is that the applicator may not be useful for all types of carcinoma of the cervix. The large fungating carcinoma of the cervix, filling a large proportion of the vault and the contracting eroding type of carcinoma or a small vagina may not permit the applicator to be used. Despite the increased range of the radium, there is still a limit to its efficacy in terms of distance from the mid-line, and although early Group 2 cases will undoubtedly be more effectively treated if they are suitable, extension well out toward the pelvic wall will still need supplementary treatment by X-ray therapy to raise the dosage to the required level.

It is not in the best interest of the patient to standardize a technique for all kinds of growth, having in mind the fact that they vary considerably, from the stenosing contracting type to the large cauliflower mass, and there is a variable extension of growth into the broad ligament on one or other side or both. It is clear that a mass in the broad ligament of large dimensions or near the lateral pelvic wall is beyond the effective range of radium however skilfully it is applied, and whatever intra-uterine and intra-vaginal apparatus may be used. The possible exception to this is a highly radio-sensitive growth, which, however, is found in the minority of cases.

Principles of treatment.—It is better to use a moderate dose of X-rays to shrink down a large growth to such a size that it brings it within the effective range of the radium, and secondly it is an obvious advantage to shrink down the primary growth if it is bleeding profusely, and causing a foul filthy condition of the vaginal vault.

A disadvantage of preliminary X-rays is that in a few cases the os is inclined to scar, and it is difficult to introduce the radium, but this can be readily overcome: The cervical lumen can be maintained artificially and more than four weeks' interval between X-rays and radium should be avoided. On the other hand, one has to balance the advantage that the os is more readily located when certain filthy bleeding growths are shrunken down and consequently the lumen is more visible. It has been claimed by some that even the large growths do shrink considerably after the first and second radium treatment thus bringing the outer part of the growth within the range of the radium for its second or third application.

This is a misleading statement because it is clear that the outer part of the growth as it shrinks has only received its contribution of dose close to the radium, possibly on the third application only, and is unequally dosed.

With regard to the application of radium all types of local growths so far as the cervix are concerned do not lend themselves equally well to exactly the same technique of radium treatment and a strong plea is made for individualization of the radium planning so that the best possible distribution of radium is used for a particular type of growth being treated.

It has long been recognized that certain types of growth whatever their situation in the body, respond better than others to radio-therapy, even though they may be situated in exactly the same part.

The soft proliferating mass is highly radio-sensitive whatever its histology. This kind of growth has an excellent blood supply, which is a great advantage in radio-therapy.

The hard infiltrating well-differentiated growth, extending deeply but slowly into the tissues in order to obtain enough blood supply to grow, is the least radiosensitive. There

is a third type of carcinoma which grows rapidly and is anaplastic. On account of its satisfactory blood supply it may form a fairly large non-ulcerating mass, or only partially ulcerated mass, near the os, and is associated with a huge mass in one or both broad ligaments. It is very radio-sensitive.

In the Royal Northern Hospital, Radiotherapy Department, the above principles guide the plan of treatment. Anything but a small growth receives preliminary X-ray therapy especially if it is not highly differentiated.

A proliferating mass is treated by a ring of radium in a rubber ring pessary-like container fixed mechanically to an intra-uterine tube. The growth fits into the ring and is evenly dosed.

An eroding cavity or stenosed vault is treated by a sphere fitting up in the vault and attached mechanically to an intra-uterine tube on a stem which passes through the sphere.

A large vault is utilized to take a large egg-shaped applicator comparable in size to Drs. Donaldson and Neary's model. I intend to use their principle of screening from now on.

Mr. Rees of the Gynaecological Department agrees with me that individualization has improved the results.

A new method of treating a mass in the broad ligament by rotation X-ray therapy focusing the X-rays accurately and offering more hope for these advanced cases is now being used at the hospital.

Mr. G. W. Blomfield: The Sheffield appliance for carcinoma of the cervix is for a single vaginal source of radium placed in the central axis. It is, perhaps, less effective in the cut off of radiation to the point generally known as "point A" but it is possibly more versatile and adaptable. It is used in conjunction with a separate uterine source and "spacers" of different sizes are used for packing the vaginal walls away from the appliance. This appliance has a spherical head of platinum giving 1 cm. screenage over the rectum reducing the dose in this direction to 25%. The main beams are directed upwards and forwards at angles which have been worked out after making a number of dissections on autopsies, the aim being to give maximal radiation to the parametrium and pelvic wall whilst not taking the rectum, bladder or pouch of Douglas above tolerance. A second applicator is now under construction, having a detachable cap which can be removed when there is difficulty in applying intra-uterine radium. This will then direct extra radiation upwards at an angle which can be adjusted to suit requirements. The vaginal radium is inserted after all else has been fixed to the satisfaction of the operator and can be removed without disturbing the appliance.

In answer to questions.—I do not think that the difficulty encountered in cases of stenosed vagina is of great moment. Those cases with advanced stenosing growth will not be cured by any technique we know of at present, whatever the type may be histologically. They require a modified technique.

The amount of radium used in the Sheffield appliance is 200 mg. of pure radium in a tube of active size 7 mm. length by 4.4 mm. diameter. The uterine source is 30 or 40 mg. total, in a separate uterine tube. The time of application is varied according to the size of the spacers used.

Previous trials, completed a year ago, with a lead appliance and two radon sources, have shown that the technique of using heavily screened radium in the central vaginal axis works clinically and makes increased dosage possible without danger, but the screenage must give adequate cut off of radiation in the correct anatomical directions.

[June 15, 1945]

Congenital Defects Following Rubella in Pregnancy.—IVOR HUGHES, F.R.C.S.

This case manifests most of the congenital lesions which have been stated by Gregg [1], Swan [2], Erickson [3] and other writers to occur when an expectant mother contracts rubella in the early months of pregnancy.

Mrs. E. contracted this disease in the second month of her first pregnancy, the infection being of a mild type. Her brother-in-law, who is a doctor, diagnosed the disease as rubella and insisted on her remaining in bed for three days although she stated that she felt well enough to carry on with normal duties. I stress this point because it has been suggested that the virulence of the unknown virus of rubella has possibly been enhanced in the war years, so producing lesions which have not been recognized earlier.

The baby was born two weeks after term (date of birth 21.11.40) and, like other cases quoted, he was small, ill-nourished and difficult to feed, pale, irritable and a poor sleeper. Weight at birth 6 lb. 6 oz.

Later a congenital cataract of the left eye was noted with enophthalmos. Nystagmus was demonstrated at a later date. This type of cataract bears no resemblance to any other type of congenital lesion of the eye described by Duke-Elder [6], Mason in 1937, Parsons in 1936 and others. Some observers note that a bilateral cataract is more common than a unilateral lesion.

Deafness was noticed as the child grew older and now deaf-mutism plus mental retardation are obvious.

He has the typical congenital heart lesion, due to a patent foramen ovale, in the inter-ventricular septum.

At present he is smaller and lighter in weight than the average child, and, in comparison with his brother, who is two years younger, appears to have microcephaly.

The boy has contracted no illness since birth which would be likely to cause any of these lesions.

The mother has had two children since the birth of this boy and both are healthy and normal in all respects. There is no familial history of any abnormality on either the maternal or paternal side.

In a survey of the literature Gregg [1] was the first to draw attention to these malformations, tracing examples back to late 1939. He recorded 78 cases but, in a small percentage of these, it was doubtful whether or not the mother suffered from rubella, and in one case mumps was thought to be the predisposing lesion.

Swan [2] and his co-workers of South Australia undertook a research for the National Health and Medical Research Council of Australia and examined 61 infants, 36 of which were found to have these congenital defects, and of these, 31 of the mothers had had an illness during pregnancy, usually in the first three months, which was thought to be rubella.

Later these observers published a further series of 10 cases in which all the mothers had suffered from rubella.

Reese [4] in America published 3 cases, Erickson [3] 11 cases, and Hope Simpson [5] in a letter to the *Lancet* described 2 cases—the only reference to the subject in this country.

In Erickson's paper in the *American Journal of Pediatrics* he states that in Gregg's series of 78 cases of congenital cataract, 44 of them had congenital heart disease also and, secondly, in his reference to Swan's papers, in which there were a total of 49 cases, 25 of the mothers developed rubella in early pregnancy and the 25 babies all had congenital defects; of those developing the disease in the third month only 50% had defects, and, after the third month, only two out of 16 of the babies manifested abnormalities.

Finally he states that in the second series published by Swan and in his own 11 cases, 100% of the offspring showed congenital lesions.

The pathology causing the abnormalities is obscure but it has been suggested that as the filtrable virus of rubella passes through the barrier of the chorionic villi at a time when lens and septa formations are occurring (i.e. sixth to eighth week of pregnancy) eye and vascular lesions are the sequelæ. Therefore the percentage of congenital lesions must be higher if the disease is contracted in the first three months of pregnancy.

Two of the writers (Erickson and Reese) suggest that, as these lesions follow rubella, it might be justifiable to terminate the pregnancy in cases where the disease has been proven. Such a course, in my opinion, could not be adopted at the present time. So far only positive evidence that rubella causes congenital lesions has been published—in other words the writers have traced back the history of rubella in cases showing the lesions. I feel that an investigation covering a large number of antenatal cases should be undertaken in order to try and discover the percentage of cases of maternal rubella in pregnancy in which no congenital lesions were subsequently manifested.

It is only by collecting both positive and negative findings that one can assess the correct method of dealing with such cases, and in order to facilitate the tracing of cases of rubella the disease should be made notifiable throughout the country.

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A Discussion on "The Use of Massage and Exercises in Pregnancy and Puerperium" was opened by Dr. Kathleen Vaughan who showed a film entitled "Childbirth as an Athletic Feat", followed by Mrs. Guthrie Smith (St. Mary's Hospital), Sister Randall (St. Thomas's Hospital) and Mr. Dick Read. Subsequent speakers were Dr. R. H. Paramore, Professor F. J. Browne and Miss Beatrice Turner. Dr. Vaughan replied.

Section of Epidemiology and State Medicine

President—P. G. STOCK, C.B., C.B.E., F.R.C.P., D.P.H.

[October 26, 1945]

Notes on Certain Trends in Public Health Work in the City of New York and in the States of New York, Massachusetts and Georgia

By MELVILLE D. MACKENZIE, M.D.

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It is impossible to visit the United States without being struck with the energy and enthusiasm with which the medical officers and nurses of the public health departments approach their work, particularly in relation to such problems as poliomyelitis, cancer, venereal diseases, home accidents and health education.

Fortunately, at the present time, the United States are in a position to back this zeal adequately, both financially and in trained personnel. Consequently great progress has been made in social medicine in America at a time when our own effort has been unavoidably limited by the war to the solution of questions less directly concerned with ordinary public health problems.

The time at my disposal only permitted me to visit the City of New York and three States. Consequently my notes are based on observations made in relation to these four areas only. No attempt was, of course, made to compare any results achieved in America with those realized in this country, but rather I studied the latest trends and methods of administration in relation to social medicine with special reference to the control of communicable diseases.

Taking first the general public health administration of the Regions I visited, the following points emerge as of particular interest.

State Health Administration.—The Health Commissioner of a City or State is not responsible to any lay representative or other committee for his expenditure but only directly to the State Governor or, in New York City, to the Mayor.

He is, however, generally associated with some form of Board of Health or Advisory Council, the constitution, powers and activities of which vary considerably in the different States. In the City of New York the Board of Health consists entirely of physicians most of whom are professors in one or other of the universities. This Board advises the health commissioner and, in addition, has comprehensive legal powers in connexion with the establishment of the sanitary code for the City and in dealing with individuals who break it. The sanitary code which is entirely prepared by this body has full legal force, with the proviso that none of its enactments are in contradiction to any of the State or Federal laws.

In some States Boards of Health recommend the health officer for appointment and have considerable legislative powers. In others the Board may be purely advisory and consist entirely of medical experts or of a majority of medical experts with a number of laymen. In other cases an advisory council may exist largely as a means of interpreting the health officer's programme to the general public and in this case is constituted by members representative of the leading social organizations of the area and individuals particularly interested in public health.

The care with which the amount of work done, the results achieved and the annual expenditure involved are estimated is a striking feature of all branches of the health work. Elaborate systems are devised and used for determining this and, moreover, through the use of health practice indices the results in any one locality are constantly compared with those in neighbouring localities and in relation both to the individual State and the United States as a whole.

The closest liaison is maintained between the staff of the health department and the universities. Members of a university staff are extensively used on a part-time basis by the health authority and conversely members of the health department staff are utilized as lecturers in their speciality in the faculties of medicine.

Clinics in general are run largely by part-time physicians who have been selected for the purpose and given special training at the cost of the health department. Such part-time doctors are given a detailed handbook covering the administrative aspects of their work and are supervised by a number of whole-time consultants who visit the various clinics and control the work generally. A medical officer of the health department is, of course, in charge of each branch of the work from the purely administrative angle.

It is interesting to note that in clinics generally, including those for tuberculosis, venereal disease and maternity and child welfare, every patient is given a card with an appointment for a definite time so that waiting is obviated.

First-class laboratory facilities are available for the use of practitioners. These are regarded not only as of great value to practitioners from the point of view of diagnosis but also as an important factor in winning the co-operation of practising physicians in carrying out the State health programme.

Much stress is laid on vital statistics and a strong statistical division is regarded as an essential part of every health body. Detailed statistical data are regularly used not only for assessing results in each branch of a health department's work but also as an aid to planning the future programme, particularly as regards the relative practical importance of the various branches of work as claimants on the budget allocation.

In the United States generally it is remarkable what powers are available in connexion with the notification and compulsory treatment of such diseases as those of the venereal group, tuberculosis, &c. Indeed many of the sanitary codes make it a crime to spread any communicable disease and this is very broadly interpreted.

The closest co-operation is invariably maintained with all practising physicians and the view is widely held amongst health officers that types of clinical activity which are intended to promote the health of the individual should be allocated to practising physicians as soon as they are willing and ready to undertake this work. Health officers make every effort to win the confidence, friendship and approval of the organized medical body of each community, and local medical societies are urged to set up a special public health committee which aids and advises the health officer in his programme and interprets his policies and activities to the local medical profession. Health officers are encouraged to become members of the local medical society and to take an active part in the affairs of that organization. The membership of the Board of Health wherever possible includes one or more representative public-spirited practitioners who assist the health officer in working out a co-operative programme.

CONTROL OF COMMUNICABLE DISEASES

Importance is attached in the United States to notification of communicable diseases as a *method of estimating the size of a problem* even if prevention or other public health activity is not directly or at the moment possible. In the State of New York which may be taken as an example, some 33 diseases are notifiable, including cancer.

It is very interesting to note that the striking reduction in the diphtheria, scarlet fever, typhoid and measles death-rates has resulted in a deliberate transfer of effort from these diseases to such other killing conditions as cancer, accidents and heart disease.

Every care is taken to ensure that epidemiologists are in constant touch with clinical cases and that some of their time is regularly spent in the wards of a hospital taking cases of communicable diseases. The epidemiologists attached to the health department act as a consulting service to practitioners and also see all doubtful cases on behalf of the health department. Their duties are concerned only with the diagnosis of the case and a public health nurse is responsible for seeing how far quarantine measures are possible in the home or are being carried out.

Extensive use is made of expert advisory committees in connexion with the control of communicable diseases generally. These experts are not members of the staff of the health department but sit in an advisory capacity only, particularly in connexion with outbreaks of unusual diseases.

Stress is laid on the maintenance of close co-operation with practitioners in the control of communicable diseases through the medium of regular letters and circulars outlining the epidemiological importance of any outbreak which has occurred and describing the facilities which are available in the health department for the use of practitioners. Similarly, when a case of infectious disease is notified a special leaflet is sent to the parent outlining the cause of the disease, the method of its spread, and describing the help that can be given by the health department.

Placarding for infectious diseases was for a time tried in New York City but is not now regarded as being of practical value. The general view is that in actual practice very little if anything is achieved by placarding and for its execution a disproportionate amount of the time of the public health staff is required.

A check is kept on notifications through the medium of the official and private laboratories. The official laboratories notify the health department of all positive specimens examined and private laboratories are only licensed on condition that this information is also supplied to the health department. In cases where no notification has been received directly from the practitioner the question is taken up with him.

The view held both in New York City and New York State with regard to infectious diseases generally is that these can be perfectly safely nursed in the wards of an ordinary general hospital, provided proper precautions are taken. All post-war hospital planning, in the case of the City of New York for example, is based on the incorporation of infectious disease sections, including tuberculosis, as parts of general hospitals.

Measles.—With regard to measles, a large amount of work is being done both experimentally and in the field in connexion with the use of gamma globulin and placental globulin. In recent work by the Department of Health of New York City gamma globulin (2 c.c.) was administered to 814 household contacts (aged 6 months to 6 years) of measles. None developed regular measles, 78.7% were completely protected, and 21.3% had modified measles. Of this latter group 92% had mild and 8% had moderate measles. In a group of 65 similar contacts receiving no prophylaxis 83% developed measles. As a result of these and other observations in New York City gamma globulin is to be distributed for children under five who are contacts to measles, particularly for use in hospital wards where a case of measles occurs.

Plague.—During my visit I was very interested to see the detailed rat proofing of the buildings at the La Guardia aerodrome at New York. This, I believe, is one of the first aerodromes to be completely rat-proofed. The importance of this in connexion with aerodromes is illustrated by the fact that on two occasions rats have arrived alive in the airport of La Guardia, transported by aeroplane. In one case a litter of rats was actually born on an aeroplane during flight.

Scarlet fever.—Decreasing importance is attached to scarlet fever as an entity and it is generally regarded as one of a group of hæmolytic streptococcal infections, including septic sore throat. Thus in New York City the reportable disease "Scarlet Fever" is now officially included in a wider classification, namely "Streptococcal Sore Throat, including Scarlet Fever". Contacts are not excluded from school or work. Visits by nurses to the homes of cases of scarlet fever are no longer required and children recovered from streptococcal sore throat, including scarlet fever, may be readmitted to school on a card issued by the health department or by a physician.

Smallpox.—With regard to smallpox, no child is admitted to school unless successfully vaccinated.

Tetanus.—In the opinion of the health authorities, the amount of tetanus in certain areas is such as to render it desirable for all children to be immunized against this disease early in life. A considerable amount of work is going forward in the preparation of a tetanus, diphtheria and whooping cough prophylactic for use amongst young children. Consideration is also being given to the desirability of protecting pregnant women against tetanus as a routine measure in some areas.

Typhoid.—The typhoid incidence rate was very low in the regions visited and this is attributed to the satisfactory water supplies, the pasteurization of milk and the close supervision of food handlers. Great importance is attached to carriers, and in the City of New York, for instance, chronic typhoid "carriers" must comply with the following requirements:

- (a) Submit specimens as often as may be required.
- (b) Report in person or by writing each month to the department of health.
- (c) Abstain from handling food, drink or dishes, nursing the sick or caring for children.

(d) Notify the health department of any change of address or place of employment; such change or occupation to be conditional on the consent of the health department.

A "carrier" remains under the direct supervision of the department of health indefinitely unless (1) the gall-bladder has been removed and satisfactory tests carried out subsequently or (2) five consecutive stool specimens taken not less than one year apart are reported as containing no typhoid bacilli. "Carriers" are in practice kept under very close supervision and are regularly visited either by a nurse or a doctor. The health departments are commonly in a position to pay up to £12 a month from health department funds in a case where the "carrier" has to change his occupation. Generally speaking operative treatment is not recommended but if a patient insists a health department will make a grant of up to £50 for the operation.

Rheumatic fever.—Rheumatic fever in the United States is regarded as one of the foremost health problems of childhood.

The object aimed at is to lessen the chances of developing the disease, to do all possible to prevent heart damage once the disease has occurred, to prevent recurrence of the infection following the initial attack, to prevent mental and emotional maladjustment in the patient and members of his family, and, perhaps most important of all, to prevent the labelling as "a cardiac cripple" of a child who has satisfactorily recovered or been erroneously diagnosed. Great stress is laid on the importance of case-finding. This is done chiefly by practitioners but also through public health nurses, school nurses and teachers, child health conferences, crippled children's clinics, social agencies and parents.

In a rheumatic fever programme a paediatrician is employed on a part-time or full-time basis and is responsible for the medical care of all children with rheumatic fever in each stage of treatment whether in a clinic, hospital, convalescent home, foster home or the child's own home. In this way continuity of medical care is assured. A medico-social consultant is responsible for seeing that any family and environmental difficulty, or the feelings of the child about his condition, do not prevent him from following the treatment recommended or getting the maximum benefits from this treatment. Finally, a public health nursing consultant is responsible for supervising the nursing services for children under the programme. Diagnostic services are provided by the paediatrician in clinics with all necessary facilities, including fluoroscopic and electrocardiographic machines. Consultative services are made available to private physicians, school physicians and county health officers.

When a child has recovered from his rheumatic infection he is encouraged to live as normal a life as possible. At the same time every effort is made to prevent a recurrence of the infection and he returns to the State rheumatic clinic periodically for medical examination and advice. Finally, great stress is laid on the education of doctors and the public both in relation to the disease itself and to the rheumatic fever programme.

A large amount of work is being done at the present time in connexion with the prophylactic use of the sulpha drugs in respect of rheumatism but the question can still only be regarded as in an experimental stage.

Tuberculosis.—Broadly speaking the methods used in the control of tuberculosis in the States I visited corresponded with those used in the progressive areas in this country. There are, however, a number of special points in American practice to which attention should be drawn.

Tuberculosis work generally is done in the closest possible association with general practitioners, and in New York City, for example, any alteration in the tuberculosis code is only made in consultation with practitioners.

All forms of tuberculosis are notifiable. In addition, in some regions, cases of tuberculosis may be removed to hospital by the health department if the continued residence of the patient in the place where he may be is considered dangerous, or likely to be dangerous to the lives and health of other persons. The patient may be compulsorily retained in hospital until the health department is satisfied that he may return to his home without risk of spreading the disease.

The clinics are in general staffed by part-time physicians, on a sessional basis, who have been specially selected and have had a basic training in tuberculosis. In the City of New York, for example, the work is carried out by 85 such part-time physicians. These doctors are required to work in accordance with a manual of administrative procedure setting out the diagnostic standards and the classification of the different stages of the disease but the clinical side of the work is left to their individual initiative.

Commercial firms are commonly employed for mass radiography which is done under contract.

"Contact" examination is along the lines generally followed in the United Kingdom, certain age-groups attending regularly over a prolonged period and others only being examined once. Importance is attached rather to the number of households infected with tuberculosis than to the number of cases.

Mass radiography is being used on a steadily increasing scale amongst industrial groups and others. The work is, broadly speaking, limited to various groups rather than extended to the whole population.

School teachers are regularly X-rayed as well as all nurses.

There is an increasing tendency to regard the sanatorium as the administrative centre of the tuberculosis service in its area, thus combining preventive and curative work. This

is well illustrated in the case of the Middlesex Sanatorium in Massachusetts. The institution, which is modern in construction, deals with in-patients, out-patients, and "contacts" in the clinics in the surrounding area. The staff of the sanatorium, both doctors and nurses, consequently spend a part of their time in the sanatorium wards and the rest in work in the clinics, including the treatment of ambulant cases, the search for new cases and the observation of "contacts". All the clinic card indexes are kept at the sanatorium. In addition members of the staff act as consultants to practitioners and also undertake a considerable amount of lecturing to local medical societies and other educational work.

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(1) The very great energy and large expenditure of money that are being put into the central and local programmes for the control of these diseases.

(2) Venereal diseases in New York City and the States I visited were not only notifiable but treatment was compulsory. Reports on every venereal disease specimen examined and found positive are sent by all laboratories, including private laboratories, to the health department concerned and it is claimed in New York City, for example, that between 90 and 95% of new infections with syphilis are brought to the attention of the health department either through notification by doctors or the laboratories.

(3) In addition to special venereal disease legislation, action is frequently taken under a general clause which exists in many sanitary codes making it a crime to spread any communicable disease. Patients are regarded as free from infection only after a specific treatment with a definite number of injections laid down by the Academy of Medicine has been completed; no notice is taken of the serum reaction for the purpose of determining freedom from infection in the case of syphilis.

(4) The basic problem in the control of venereal disease is considered to be education and very great efforts are made to bring the necessary information to the notice not only of the laity but of all practitioners.

Among the facilities offered free to the general practitioner by the health department are laboratory examinations, lumbar puncture, clinical consultative service, provision of anti-syphilitic drugs, epidemiological service in connexion with contacts and post-graduate instruction.

A beginning has been made of teaching facts about venereal disease both in coloured and white schools. The instruction is given in biology classes and, in the case of coloured children in some areas, begins at the age of 14 and with the white children a year or so later. A considerable amount of experimental work in this connexion has already been done and the work is being expanded.

(5) There is a feeling that in the past in clinics in the United States, too much energy has been devoted to the long-continued treatment of non-infectious persons, who may constitute 85% of those attending the venereal disease clinics. At the present time, efforts are being concentrated largely on the search for cases, the examination of "contacts" and the treatment of patients so as to render them non-infectious as rapidly as possible. When a doctor has notified a case he is asked by the health department whether he desires to treat the case himself and whether he is willing to ascertain the names of the contacts. If he declines the former the case is compulsorily treated in a clinic until it is free from infection. If the doctor does not wish to trace the contacts, this work is done by a public health nurse. It is interesting to note that men are commonly employed to follow up male contacts.

(6) Both pre-marital and pre-natal examinations are compulsory in many States. In some States blood examination is also required in the case of workers in industry. If an individual is found to require treatment he is allowed to continue his work conditional on completing a prescribed course of treatment. Some commercial companies insist on the whole staff from the President of the Board downwards undergoing regular blood examinations.

Widespread blood examinations are being pushed by the Chambers of Commerce with a view to preventing physical and mental disabilities which might interfere with a man's work and also in order to avoid possible compensation claims. The results of these sera examinations are interesting. Thus 399,218 individuals were examined by

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the laboratories of New York State during one year. By this means 7,659 individuals or 1.9% of the total were found to be positive.

With regard to pre-marital examinations, from a random sample number of 2,887 in New York State 1.2% males and 1.3% in females gave positive serological reactions.

Examination of restaurant workers is optional in some areas but compulsory in others. (7) A considerable amount of work has been done in connexion with the provision of prophylactic facilities but in the civilian population these have been found to be hardly ever used and are not considered to be of practical application from an administrative point of view.

Cancer.—The ideal aimed at is "the prevention of 50% or more of the hundred thousand deaths from cancer which are occurring annually in the United States". The great expenditure of both energy and money in the cancer control programmes has already given very striking results. These are shown by the following figures in the two areas studied.

In the State-aided clinics of Massachusetts the shortening of the time between a patient first noticing symptoms of the disease and presenting himself to a physician has been used as one measure of the effectiveness of the cancer programme. In the early years of the programme this delay averaged 6.5 months. Between 1936 and 1939 it was 5.3 months and in 1940 4.6 months. Since this date a further fall has occurred bringing the time down to 3.2 months, or *half that of earlier years*.

The second period of delay is that between first consulting a physician and visiting a cancer clinic. This delay has been decreasing rapidly and is *now about half what it was in the early years of the clinics*.

The third delay is between presentation at a clinic and the beginning of treatment. At the present time about *two-thirds of the patients are treated within one week and over 90% within one month of the first clinic visit*.

In the State of Georgia the effect of the cancer control programme is shown by the considerable increase of patients presenting themselves at cancer clinics who are found not to be suffering from the disease. Thus in the year 1937, 81.2% of all the cases presenting themselves at State-aided clinics were malignant, whilst, in 1942 only 59.5% were malignant. This percentage has continued to fall steadily but the corrected figures for later years are not yet available.

Briefly the programmes which have resulted in these striking results are based on: (1) Early recognition. (2) Notification. (3) Provision for free and early treatment. (4) Search for new cases and "follow-up" work. (5) Intensive education of physicians, public health nurses and the laity, including instruction in the higher classes of schools. (6) Research.

Home and farm accidents.—Great energy is being displayed in America in the prevention of accidents in the home and on the farm. In considering deaths for all causes and for all age-groups in the United States it will be found that accidental fatalities of all types are third in numerical importance. For the country as a whole in 1941 there were more deaths from accidents in the home than motor vehicle deaths (30,000 as compared with 28,200) and nearly twice as many as from industry or public deaths due to causes other than motor vehicles. In 1942 in New York City accidents were the principal cause of death of all children from 1 to 14 years and in the age-group 5 to 9 years deaths due to accidents are almost as great as the deaths from all diseases put together.

As an example of the importance attached to this work mention may be made of the organization set up by the Health Department of the State of New York which works along the following lines and which may be regarded as typical.

A Home and Farm Safety Advisory Committee has been set up by the Division of Public Health Education.

It works through a number of sub-committees covering research and statistics, legislation, household safety, personal health and safety, finance, farm safety, safety in housing and safety to children in farm work. Technical brochures are sent to all architects and engineers regarding safety of construction in houses. A similar booklet exists with regard to electrical fittings in which stress is specially laid on the importance of plugs being at a height inaccessible to children, safe wiring, and the avoidance of shock hazards in washing machines, electrical toys, &c.

A circular is sent to every practitioner inasmuch as "preventive medicine is definitely a part of a physician's practice and the prevention of accidents, especially in the home, is an important part of his work". A committee of physicians on personal health and safety has been set up which amongst other activities draws the attention of medical practitioners to such physical conditions as may cause accidents in the home, i.e. defective eyesight, impaired hearing, muscular inco-ordination, dizzy spells, night blindness, crippled conditions, epilepsy, &c.

Perhaps the most important work is done by the public health nurses who work in accordance with the "Home Safety Manual for Public Health Nurses". This is an excellent document explaining in detail the causes of accidents in the home. These may be due to:—first, faulty design of the house (faulty construction of stairs, improperly lighted steps, insufficient overhead clearance on stairways, faulty construction of stair rails, insufficient light, disorder, faulty planning of kitchen space, too few exits, doorways too near steps); secondly, neglect of maintenance (defective stair covering, ice on steps, slippery

cracked linoleum, insecure screen fastenings, loose plaster, broken chair rungs, &c.); thirdly, faults in electrical maintenance (using electrical appliances in damp location, overloaded circuit, frayed cords, using fuses of too great capacity, faulty washing machines, over-heating of electric irons, over-turning of electric heaters, unprotected whirling plates of electric fans, &c.); fourthly, lack of skill (floor left slippery after waxing, using substitutes for ladder in curtain hanging, mis-use of knives, cooking steam, bursting of canning jars, botulism in food preservation, improper position in heavy lifting, explosion during dry-cleaning, leaking gas). The booklet also deals with the danger to children of suffocation, choking, burns and scalds and also stresses the importance of the protection of the aged against accidents so as to obviate their becoming a burden on the rest of the family. In the case of the aged attention is particularly drawn to the avoidance of falls (slippery walks, stairs without handrail, slippery bath tubs, poorly lighted stairways, high beds, defective sight). The public health nurses systematically visit houses drawing attention to defects which may be the cause of accidents and, at the same time, distribute to householders popular booklets on the importance of accidents in the home and their prevention. In addition to wireless talks and other means of publicity much educational work is done through the medium of the schools, especially through the Junior Safety Voluntary Movement.

PUBLIC HEALTH NURSES

The work of the public health nurses is amongst the most interesting features of the health work in the United States.

Although her visit usually originates in connexion with a case of sickness, the whole approach of the nurse is *to the family rather than to the individual*. In addition to giving nursing attention to the patient the nurse invariably takes the opportunity of dealing with other health problems in the home such as cleanliness of the house and the children, their food, clothing and sleeping habits, as well as defects in the house itself. She also explains where any medical facilities that the family may require are available and gives information on such points as periodic health examination, immunizations, accident prevention and the prevention and recognition of early symptoms of such diseases as diabetes, cancer, orthopaedic defects, rheumatic fever, tuberculosis and syphilis. Since the health of one member of the family may affect directly or indirectly all the others, the public health nurse considers primarily what help can be given from a family point of view.

HEALTH EDUCATION

In the United States very high priority in public health work is invariably given to health education, including that of practising physicians and the laity as well as to regular in-service training of public health officers. It is held that "no public health programme can be completely successful in the United States without the confidence and support of the people who benefit by it".

The public health education of the practitioner forms to an increasing degree an important part in the curriculum of the medical schools, and, after qualification, widely varying courses of post-graduate study are available. Handbooks on certain specified diseases are sent to every practitioner by health departments, e.g. manuals on cancer, venereal disease, &c., as well as a brochure outlining briefly what the work of the health department is and stressing particularly the ways in which the department may be of assistance to him and how to avail himself of this help.

The greatest attention is paid to the in-service training of the staff of the health department. After or before appointment doctors, nurses and sanitary personnel are sent for special courses at a university and are also given intensive training in the activities of the health department itself before taking up their work. During their time of service, study leave is given to technical members of the staff of the health department and through the payments of expenses, &c., the staffs are encouraged to attend National and Inter-State conferences.

Health education of the laity may be divided into that done in the schools and that done amongst the adult population. The health department works in the closest association with the education department, often with a joint committee. The health syllabus for school teaching is exceedingly comprehensive and covers all grades. It is interesting to note that a beginning is being made in the teaching of certain aspects of cancer and venereal disease in schools. One method of health education which is extensively used is to give children written questions and ask them to consult their parents with regard to the answers, thus carrying health education into the home itself through the school.

In the case of adults every possible method of publicity is utilized and the relative values of the different methods employed are constantly assessed. The health education department in a City or State forms a separate division of the health department. In New York State for example the division of health education has a director and two assistant directors with the following sections:

Publications (sub-sections for medical editing, representation of staff, bulletin, illustrating and distributing, designing of posters and general art work, charts and graphs).

Information Service (health education institutes, public addresses, field health education, local and general health programmes).

News releases (sub-sections for local publication, feature articles, cartoons, press photographs).

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The news releases by the health department are on the same scale and during 1944 in New York City of the 42 news releases from the health department one or more was used by 391 newspapers in the city and constituted the basis for 1,825 items.

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A visitor to the United States cannot fail to be struck by the cleanliness with which food is prepared and served even in the case of inexpensive restaurants. Apart from the very careful supervision exercised over purity of food products, the health department closely supervises hotels, restaurants and bars from the point of view of cleanliness in cooking and serving.

Bacteriological swabs are regularly taken by inspectors of the health department from utensils including glasses on the serving tables of restaurants and cafés and the average plate count per utensil-surface examined must not exceed 100. Higher counts are presumptive evidence of inadequate cleansing or recontamination by handling or during storage and are consequently a breach of the sanitary code and dealt with accordingly.

Restaurant keepers must supply their employees with at least one clean overall daily both in the service rooms and in the kitchens.

Milk may only be served to customers from sealed bottles opened by the customer himself.

It has been exceedingly difficult to summarize the information I gathered in the time available. Fortunately, I was able to collect a very comprehensive documentation of some 300 books, publications, and pamphlets, covering in detail the various points I have referred to. This documentation is in my office at the Ministry of Health, and I shall be most happy to make the relevant sections available to any member interested in any particular problem or desirous of giving consideration to the possibility of applying it in his own work.

In conclusion I sincerely hope that as soon as ever circumstances permit it may be possible for many of my colleagues to go to the United States and avail themselves of the invariable kindness and generosity of the Americans in putting at our disposal full information regarding their technical progress and administrative experience.

Section of Urology

President—F. MCG. LOUGHNANE, F.R.C.S.

[June 28, 1945]

Some Surgical Aspects of Urinary Bilharziasis

By R. OGIER WARD, M.Ch., F.R.C.S.

BILHARZIASIS is a disease which produces many important changes in the urinary tract and is, if only for that reason, worthy of the interest of urologists. The main object in this paper is to direct attention to the fact that patients with the symptoms of this disease, typical or obscure, may be expected to make their appearance in the hospitals of this country during the years which lie immediately ahead of us, for British troops have served in countries where bilharziasis is ever present, and many have undoubtedly been infected with it. Napoleon's troops who served in his march to the Pyramids suffered from hæmaturia, which was undoubtedly of bilharzial origin. In "Notice sur l'hématurie qu'éprouvent les Européens dans la haute Egypte et la Nubie" A. J. Renoult, médecin, chirurgien, majeur de la gendarmerie d'élite, has something to say on this subject. His paper was read at a meeting "en messidor, an onze" and was published in the *Journal Général de Médecine, de Chirurgie et de Pharmacie* in 1803. Renoult says: "Elle parut affecter plus particulièrement les cavaliers, n'épargne même pas les chevaux; ses ravages se portèrent principalement sur les plus jeunes." He believed that it was caused by excessive sweating, forced marches, and riding horses "vifs et fougueux".

The cavalry were probably more affected than the infantry because they were exposed thrice daily to the risk of infection when watering their horses. I may remark that as a gunner officer in the Suez Canal Zone in 1915 such waterings were my almost daily duty, and I remember the strict orders prevailing against anyone getting into the branch of the so-called Sweet Water Canal allotted to us. I would like to add that I am certain—for I was already a budding urologist—that none of our horses suffered from hæmaturia. Renoult's observations that the younger soldiers were chiefly affected is probably to be explained by the fact that the old soldiers with twinges of rheumatism in their back muscles are but little thrilled by the opportunity of a bathe. Renoult noticed "les urines rares, épaisses et irritantes", also that "leur âcreté doit se faire particulièrement sentir sur les veines qui rampent le long des parois internes de la vessie". He treated his patients with abundant drinks but he sadly remarks that: "mais chez un aussi grand nombre l'hématurie est devenue si rebelle qu'elle ne leur laisse que la triste perspective d'une vieillesse toujours souffrante." During the South African War 625 cases became infected and a few were met with amongst soldiers returning to England. In 1911, 359 men were still drawing pensions amounting to £6,400 per annum, whilst there were others who had already been permanently pensioned on account of the disease. In the war of 1914-1918 there were more cases, and in 1915 a Commission under Professor R. T. Leiper had been sent to Egypt to study bilharziasis, and later published a valuable report and proved the correct method of its transmission. A considerable epidemic occurred in 1916 amongst Australian troops. Sir Philip Manson-Bahr, to whom I am very specially indebted for much help in the preparation of this paper, help from his book on "Tropical Diseases" and help given personally, was in Egypt at that time. He has told me about the incident, which he and N. H. Fairley investigated. The Light Horse had returned from Gallipoli in 1916 to the camp established for them at Tel-el-Kebir, a place which lies on the Eastern border of the Nile Delta and is about half-way between Cairo and the Suez Canal. Here they found a welcome chance of bathing in one of the main irrigation canals, and the troops who did so quickly began to suffer from skin irritation with an urticarial rash and an irregular temperature.

At that time very little was known about the transmission of the disease and still less about its treatment. For example, in Thompson-Walker's "Genito-Urinary Surgery" published in 1914 there is a good chapter on bilharziasis. To-day it seems strange that he pointed out that it was uncertain whether infection occurs through the stomach, the anus and urethra or through the skin. As to treatment it is frankly stated that "there is no known method of destroying the Schistosoma".

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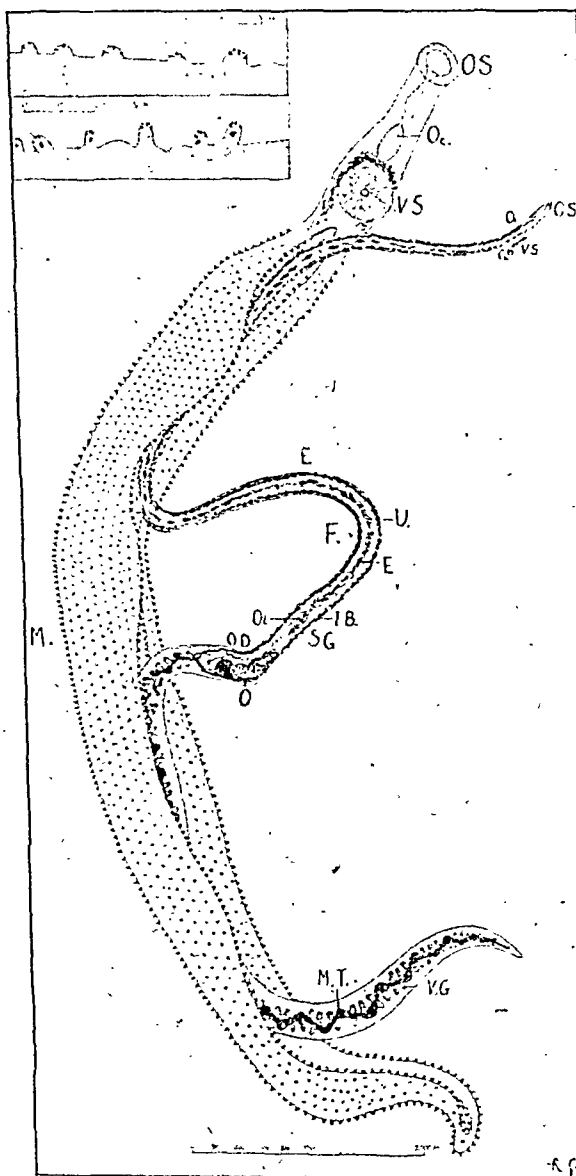


FIG. 1.—Male and female *Schistosoma haematobium* Bilharz, 1852. M., male; F., female; E., egg; G.P., genital pore; I.B., intestinal branch; M.T., median trunk; O., ovary; O.D., oviduct; Oe., oesophagus; O.S., oral sucker; O., ootype; S.G., shell glands; U., uterus; V.G., yolk glands; V.S., ventral sucker. Insets, highly magnified parts of the skin of male.

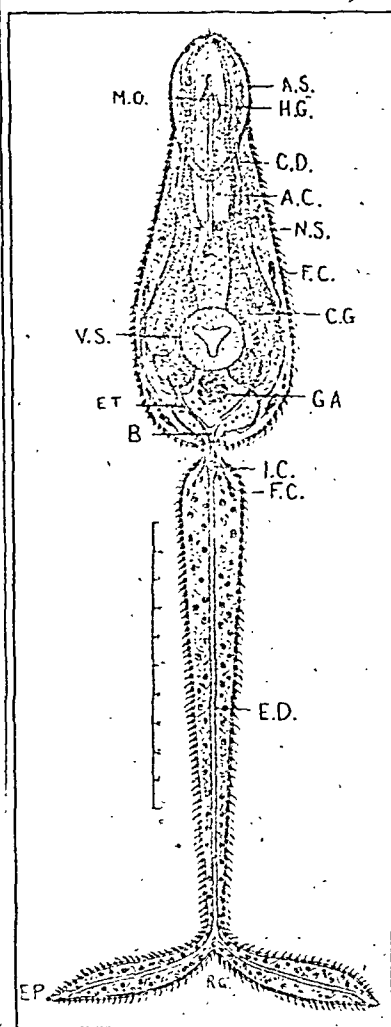


FIG. 2.—Fuller developed cercaria of *Schistosoma haematobium*. A.C., alimentary canal; A.S., anterior sucker; B., bladder; C.D., cephalic gland ducts; C.G., cephalic glands; E.D., excretory duct; E.P., excretory pore; E.T., excretory tubule; F.C., flame cell; G.A., genital anlage; H.G., head gland; I.C., island of Cort; M.O., mouth opening; N.S., nervous system; V.S., ventral sucker.

blood cells. The male worm (fig. 1) is 1 to 1.5 cm. long, and about 1 mm. thick. He is provided with two suckers both of which are near the head end, and he uses these and the projections on the skin to provide himself with temporary attachments to the vessel wall and for movement. Throughout the greater part of its length the body of the male is split to form the gynæcophoric canal, and in this the female is embraced. The female is thinner than the male and about 0.5 cm. longer. She also has two suckers, one at the extreme head end, the anterior sucker, and another close to it known as the

During this war our troops have served in Egypt, East Africa, West Africa, and Rhodesia and the Union of South Africa, all countries in parts of which *Bilharzia hæmatobia* is indigenous. It is certain therefore that now, and perhaps still more frequently when the war is over, cases of this disease both in its acute condition and at other stages are to be expected in civil practice in this and other countries where usually it is never met with.

In this war I have served for two years in Egypt, and also for two years in East Africa where the disease is common in the native troops, and as a result I have acquired some knowledge of the manifestations of bilharziasis. This paper is, however, not written about my personal experience, and any value that it may possess is because it is a symposium of knowledge gathered from others who have had much longer experience, and whose names I shall mention. Officers in charge of medical and surgical divisions in East Africa and their officers, all working under the direction of Brigadier R. P. Cormack, D.M.S., E.A.C., and supervised by Brigadier E. R. Cullinan, the Consulting Physician there, and by myself whilst I was Consulting Surgeon in that Command, have recently made some notable contributions in the investigation of this disease, and also as to the immediate effects of treating large numbers of infected, though often uncomplaining, natives. The study of the results of ultimate cure will obviously take much longer to complete.

Discovery of the Parasite of Bilharzia.

Bilharz, a German who was Professor of Zoology in Cairo, discovered the parasite in 1851. Working on monkeys and later on man he demonstrated the worms in the portal veins of both. Another name which is widely used is *Schistosoma* (*Schistos* = divided, and *soma* = body), an allusion to the longitudinal split in the male which forms the gynæcophoric canal. There are three main species of Bilharzia: *B. hæmatobia*, the cause of the genito-urinary disease which we are now considering; *B. mansoni* the cause of one disease known as Egyptian splenomegaly, and also of another variety which is intestinal bilharziasis; *B. japonica* the cause of Eastern bilharziasis. This last variety, which affects chiefly the liver and spleen and is characterized by ascites, is confined to the territories which border the Western shores of the Pacific. The ova of the Eastern disease, *B. japonica*, are discharged in the fæces, as they are in the mansoni variety. *B. mansoni* has a somewhat similar distribution in Africa to hæmatobia, but unlike the other two forms it is also found in the north-eastern part of South America. After this war cases of all three varieties may appear in our clinics, and more than one may appear in the same patient. Therefore, when we are treating urinary bilharziasis we should cause examinations also to be made for *B. mansoni*, that is to say, we should send fæces for examination as well as the urine.

In this paper only *B. hæmatobia* is discussed.

In West Africa it occurs in the British territories of Sierra Leone, the Gold Coast and Nigeria. It is found all along the North Coast of Africa, also in Cyprus, and in a few places in Arabia including the Aden Hinterland and in Iraq. As for the remaining parts of Africa, the east and the south, it is often said that *B. hæmatobia* predominates in those territories whose waters drain into the Indian Ocean, the largest river being, of course, the Zambesi, whilst in the Congo basin the mansoni variety abounds. Though this statement is not completely accurate it has some clinical importance; anyone in Natal, Rhodesia or the Union will warn you of the prevalence of hæmatobia, and as soon as you cross the Congo-Nile divide into the Belgian Congo you will find that where people speak of "Bilharzia" they are referring to the commoner intestinal variety. In Uganda and Kenya *B. mansoni* is much the commoner disease, *B. hæmatobia* being chiefly, though by no means exclusively, found in the coastal area. Dr. Plum of the Colonial Medical Service found that about 50% of the population there had blood and eggs in their urines. Others have given higher figures, but it is difficult to decide the proportions of each disease for the rectal variety produces no dramatic symptoms such as hæmaturia, and probably 30% of the population of East Africa suffer from it, the majority quite uncomplainingly. In Egypt a large proportion of the population suffer from both diseases all their lives. *B. hæmatobia* has a wide distribution in the south-eastern parts of Africa. The region of the Cape is relatively free, yet L. B. Goldschmidt, the urologist practising in Capetown, tells me that of his European patients about one in fifty is admitted to a nursing home on account of this disease, or when under treatment there for some other condition is then found to be infected.

Life-history.

The life-history of the parasite of *B. hæmatobia* may be summarized as follows: The male and female worms having developed within the liver of man next migrate to the portal and mesenteric veins, particularly the inferior mesenteric. They live on the red

considered that it cannot live in the highlands, where the cold streams run down from the glaciers of Mt. Kenya. The snail host—*Planorbis*—of *B. mansoni* has, however, been found as high as 8,000 ft. in Kenya. Be that as it may, at any height above 6,000 ft. one does not hesitate to wade when fishing for trout. In Ceylon a snail of the *Bullinus* genus is said to exist, but *B. hæmatobia* does not occur. This seems curious, for long before the East African troops of this war trained in that island on their way to attack the Japanese in Burma, and in so doing may have shed miracidia into the streams, Arabian traders must have passed between Ceylon and Africa. There are species of *Physopsis* and *Bullinus* in many parts of the world, but most do not attract the miracidia. The ovum when washed out in the urine has to take a chance, but, if it is favoured by fortune, it does find and then attack the snail, boring its way through its antennæ and thus eventually obtains its objective, which is the liver or digestive gland of that mollusc.

Whilst resident in the snail's liver, sporocysts (fig. 8), which are transparent, tubelike bodies, are developed in large numbers from the miracidium. Within about fourteen days the next stage, the cercaria (fig. 9) (*κέρκος* = tail) is developed within the sporocyst. Eventually the snail dies of his disease, but before this occurs these cercariæ are discharged from it into the water. Under the stimulus of daylight they are puffed out in clouds from the snail's pulmonary cavity. This stage of the parasite, the cercaria, which is about twice the size of a bilharzial egg, swims by means of a bifid tail. The cercaria penetrates the human skin by means of a (lytic) destructive substance secreted by special penetration glands at its cephalic end, the part selected being usually that covering the legs of some man wading in the swamps, canals or rivers; or they may presumably get into a rat, mouse or monkey. Now they lose their tails and, travelling through the lymphatics and the blood-vessels, they reach the liver of the definitive host, and there develop into the male and female worms. This last phase, beginning from the time of entering the skin, takes about six weeks, and thus the astonishing life-cycle is completed.

Most of the research upon these parasites has been done in Egypt, an ideal land for their cycle. The disease can be proved to have existed there since the 20th Dynasty, that is 1250—1000 years B.C. Sir Marc Armand Ruffer, when he was working in Egypt on tropical diseases in 1910, examined six mummies of that dynasty. He soaked some of their organs and softened them in a solution containing glycerine. Then he cut microscopic sections and found terminal spined ova in the straight renal tubes of two mummies, this is particularly remarkable inasmuch as the kidneys are not so intensely invaded as the bladder. He did not examine the bladders because he judged them unsuitable for this method. Dr. J. G. Willmore of Queen Mary's Hospital, Roehampton was working with him at that time as a junior assistant, and tells me how he saw these preparations on many occasions.

In 1910 no one knew the life-cycle of the parasite, and even up to more recent dates it was believed that the disease entered the body through the urethra. The ancient Egyptians devised a cage to protect the penis. In the last war British troops in Egypt were advised to employ more modern methods. No doubt the Army Order containing the preventative instruction occasioned a good deal of ribald mirth, but this venerable Egyptian precaution has a sound basis, for Leiper remarks that in Egypt certain leeches sometimes enter the urethra and cause bleeding from it. No one seems to have attempted to protect the female sex at any time.

In recent years the disease assumed extremely serious proportions in Egypt, and it was estimated in 1939 by Scott, a Director in the Public Health Department of the Egyptian Government, as a result of 40,000 examinations, that half of the population resident in the lowest and widest part of the Delta of the Nile suffers from *B. hæmatobia*, and very large numbers are also infected with the mansoni variety. In that country the disease seems to have increased since more efficient methods, and in particular the building of the great Nile dams, have led to the irrigation of large tracts of the Delta throughout the year, instead of only during the periods of the Nile flood as in the years prior to 1820, and ultimately its ravages led to a serious shortage of labour. In 500 male autopsies Ferguson found that 8% died of bilharziasis. As a consequence of this a special activity was developed on the part of the Egyptian Medical Services in treating the disease amongst the fellahin, particularly in the children. *B. hæmatobia* has never been so great a menace to the native's health in any other country, and this is doubtless due to the peculiar methods of agriculture which prevail in Egypt. Nor in other lands does the disease commonly give rise to the advanced pathological conditions with which the surgeons of Egypt are so familiar. The cause of this difference is not clear, perhaps it is the constant and heavy reinfection of the fellahin which decides

ventral sucker, and immediately posterior to this is the genital opening from which the ova are discharged. Brigadier N. H. Fairley, now Consulting Physician to the Australian Forces, with Manson-Bahr during the epidemic amongst the Australians in 1916 worked out the manner in which the ova leave the female by making studies upon artificially-infected monkeys, the mesentery being exposed under anaesthesia. They observed the male embracing and fertilizing the female working his way by means of his suckers against the blood-stream of the portal vein, and thence along the mesenteric veins and its branches. He is impelled to undertake this arduous journey by an instinct derived during uncounted ages in order to ensure that his progeny may reach fresh water. Presently he enters a vessel near the bladder, but still at some distance from the mucosa, but one that is too small to admit of his further progress (fig. 2). Here his more slender mate slips from his embrace and continues to advance. The exact fate of the male is undetermined, and no one seems very interested in it. But sometimes the female rejoins him, and Christopherson and Fairley have recorded remarkable cases in which without reinfection the worms have existed in a patient for as long as thirty-seven years. The female now, by using her suckers, moves forward head first until she completely plugs and so tightly stretches a small venule that no blood can get past her. From her genital opening which is close to the ventral sucker she now deposits her eggs in a chain (fig. 3), retiring little by little in the process, and thus allowing the vein to collapse upon them. This collapse ensures that the ova, which have been laid so that their terminal spines are directed downstream, are given a tilt when the blood-stream is resumed and thus the spines become imbedded in the venule's walls. These eggs are minute—0.16 mm. by 0.06 mm.—that is to say about a third the size of a cheese-mite. Twenty or more ova may be deposited by one female on one occasion. In the course of the disease millions of eggs may be laid, and a heavily infected patient may discharge in the urine more than a thousand eggs a day. The egg-laying field of choice is the vesical submucous layer, few eggs are deposited in the muscular coats. Many eggs are also laid in the submucosa of the prostatic and penile urethra, as well as in other tissues of the genito-urinary tract. The spine being imbedded prevents the ova being washed away and some say that it is, by means of the spine that the vessel wall is perforated, others hold that the ovum escapes by the action of an enzyme which it secretes and which digests away a portion of the vessel wall (fig. 4). Clearly the ova at this stage have not yet reached the epithelial layer of the vesical mucosa. It is not known exactly how they do reach it but probably the muscular contractions of the bladder and the penetrating value of the spines bring it about that a large number of them eventually work their way to their appointed destination. Under experimental conditions in monkeys this may occur in a few hours. It is at this stage that the characteristic bilharzial tubercle (fig. 5), which is about the size of a pinhead, makes its appearance in the bladder mucosa, each tubercle consisting of a collection of perhaps twenty eggs.

At this stage each ovum contains the unhatched miracidium (fig. 6) which is the next unit in the parasite's life-history. There is some evidence, as pointed out by Ferguson when Professor of Pathology in Cairo, that the miracidium whilst it is still living within the ovum, produces some toxic substance which exudes and by causing destruction of the tissues in immediate contact enables the live ovum to escape into the urine. Soon after this liberation, if all has gone well, the ovum may find itself in suitable water, and the next venture begins. The difference in the osmotic pressure of the new environment causes the envelope of the ovum to rupture, and thereby the miracidium escapes. Nature has arranged that this does not occur in normal urine, but it should be noted that the hatching can be produced artificially by adding water to the urine. A. H. Harkness had a patient who achieved this for himself by drinking three pints of beer in quick succession, the urine which he then passed was so dilute that active miracidia were found to be disporting themselves in it in large numbers. Manson-Bahr has also seen this happen. This embryo—the miracidium—contains many germ cells, and it swims in the water by means of the cilia with which it is covered. Some primeval impulse attracts it to the intermediate host, a certain water snail, the *Bullinus contortus* (fig. 7) or to other varieties of that genus. This attraction appears to be chemiotactic and absolutely specific for a suitable type of snail. The miracidia is not attracted but actually repelled by other snails which do not offer a suitable nidus. This snail must be reached within thirty-six hours if the life-cycle is to continue, but it does not inhabit every stream in Africa. It abounds in the stagnant waters of the Delta clinging to aquatic plants, stones and posts. It cannot live in brackish water. It is rare in the Congo basin. It is particularly common in the shallow Great Lakes of Uganda, and others which drain into the headwaters of the Nile, though rare in Lake Victoria, a stretch of water so vast that perhaps the storms which sweep across it make its shores uncongenial to snails. In Kenya the snail is common near the coast but it is usually

INITIAL SYMPTOMS

When man is attacked by the cercaria he suffers immediately from a severe itching involving those parts which have been immersed. The irritation may be bad enough to cause him to leave the water. This is known as "Swimmer's Itch". A vesicular rash may appear, and following this the temperature becomes irregular, this may last five to six weeks and may resemble that of typhoid. After four to six weeks an urticarial rash occurs in patients in whom the infection has been very heavy and who are susceptible. It covers the whole body with areas of giant urticaria, and is generally considered to be a toxic manifestation. An eosinophilia appears with the urticarial rash rising to 10%, or even as high as 70%, varying not so much with the intensity of the infection as with the degree of the patient's response to it. It may be remarked that a leucocytosis of 50,000 to 60,000 also occurs. In a clear case now is a good moment to begin treatment with antimony, and without waiting for ova to be found in the urine. Pain in the liver is another symptom, due to its reaction to the invaders, a reaction by which many of them are destroyed. When the disease has invaded the bladder wall the patient presently suffers from hæmaturia. This may begin at any time from three months to two and a half years after infection. It is scanty and occurs at the end of micturition and is due to the rupture of small vessels brought about by bladder contractions. It is quite painless and in an uneducated patient attracts little attention. If the invasion of the bladder is rather more severe there may be slight frequency of micturition and a slight pricking sensation in the urethra.

Some lassitude and backache may occur as the disease of the bladder progresses, but it is usually only after a very long period that characteristic symptoms of cystitis develop. Anæmia is rarely obvious except in severe cases and when sepsis has become intense.

Examination of the urine.—The most general method of making a diagnosis of *B. hæmatobia* is to examine the last few drops of urine passed, or the centrifuged deposit of the urine of the patient, under a $2\frac{1}{3}$ inch or $1\frac{1}{6}$ inch objective. No staining is required. The ova with their terminal spines are easily recognized. They may be alive, dead, or sometimes calcified. Dr. Willmore considers that a specimen of urine is more likely to contain ova after exercise, and frequently gives the patient a spell upon the exercise bicycle before micturition. Until cystitis has occurred, and this is late in the disease, the urine except for the last few drops is clear to the naked eye unless blood be present. Until the disease is advanced abdominal and rectal examinations reveal no abnormalities. In the late stages the sclerosed bladder may be palpable in an emaciated patient, and *per rectum* extensive induration may be found to involve the prostate and vesicles, and all tissues at the bladder base and in the perineum. Cases in this country are, however, quite unlikely to show any such changes. The absence of such general signs adds to the importance of cystoscopy in diagnosis.

The importance of cystoscopy in diagnosis.—The finding of the ova in the urine of course proves the existence of the disease, but it must be realized that a failure to find them does not exclude it. The D.M.S. East African Command, Brigadier R. P. Cormack—as I have already mentioned—has formed a research committee to stimulate and control investigations in military hospitals. One object was to assess the value of cystoscopy as a means of diagnosis, and the officers under his command in medical and surgical divisions have by systematic investigation of large numbers of cases amongst African soldiers proved certain facts which may usefully be summarized here, for they are not generally known outside expert circles: (1) A solitary examination of the urine for ova is a quite unreliable test, for ova are not continually released from the lesions of the mucosa. (2) Five consecutive morning specimens, the last few drops of the urine being collected and centrifugalized, will in about 85% of cases show either ova, or red blood cells, the latter being strong evidence in the mass examination of natives that bilharzia is present. (3) Even in the absence of ova or red blood cells the continual presence of pus or of albumen in a native's urine means that a diagnosis of bilharzia is probable until it has been disproved. (4) Cystoscopy is the most accurate method of diagnosis in all active phases of bilharziasis. Moreover there are several characteristic vesical changes which persist when the active stages of the disease are past. It may be argued that cystoscopy does not reveal lesions of the kidneys and the urethral mucosa; that must be admitted, but it is probably very rarely that these tissues are affected without the bladder being also involved.

Cystoscopy is therefore a procedure which should never be omitted in a case which is suspected of *B. hæmatobia* but in which no ova have been found. I myself have cystoscoped many patients with active bilharzial cystitis both in Egypt and East Africa, whose urine examinations have been negative for ova. Nor should cystoscopy be

it. But we in this country must not assume that, because one of our people has acquired the disease elsewhere than in Egypt, it will, therefore, take a less serious form. An interesting point arises here—the children of Israel, when in Egypt, lived in the Land of Goshen (that is until Moses persuaded them to rebel in about 1300 B.C., possibly against Merneptah, son of Rameses II). This was the name given to an area in which Tel-el-Kebir to-day occupies roughly a central position. As has been mentioned the Australian troops contracted the disease in that very region in the last war, and it must always have abounded in these parasites, so that it seems certain that the Israelites cannot have escaped infection. It may seem strange, therefore, that amongst the various diseases, and the cleansings prescribed for them, particularly in the books of Exodus, Leviticus and Numbers, there is no mention of blood in the urine. Perhaps the explanation lies in the fact that the legal matter in these writings is much later than the narratives and is considered to have been chiefly composed and added at about 300 B.C. By this time, perhaps 1,600 years after the Exodus, the disease would obviously be rare amongst the Israelites, for the only part of Palestine in which it occurs is around Jaffa, and it would, therefore, not be considered worthy of mention by the priesthood. Another explanation is provided if we accept the opinion of certain Bible scholars who consider that the sojourn of Israel in Egypt is purely legendary.

Some knowledge as to the existence of bilharziasis in ancient Egypt may be gained from a study of certain papyri. I am greatly indebted for information on this subject to Professor Battiscombe Gunn, Professor of Egyptology in the University of Oxford. Six papyri dealing with medical matters are known to Egyptologists. The papyrus discovered by Professor Ebers in 1875 and known by his name is by far the most important of these. It is 20 metres long and 30 centimetres high. It is possible to fix with considerable accuracy the date of its compilation as approximately 1550 B.C. The contents have almost certainly been written by a professional scribe; they were already of considerable antiquity when he did this, and it may well have been a unique assemblage of material made for the use of a practitioner of those days. The original authors of the various portions of the papyrus were no doubt themselves physicians, for these formed a quite definite professional class in ancient Egyptian society, though they had to be magicians as well as medical men, since a large part of the treatment of diseases consisted in a recitation of spells and of magical rites. Much of the papyrus is devoted to lists of prescriptions consisting of various plants, parts of animals, minerals, liquids, and other components, but it is by no means all of this character; for example, it contains a lengthy dissertation upon the heart and the blood-vessels, in which occurs the statement that "when any physician, any surgeon palpates the head, hands, abdomen, feet, &c., he examines them because of the heart, for all the limbs possess its vessels, the heart speaks out of the vessels of every limb." This seems to suggest some considerable understanding of the vascular system.

The detailed translation of a document is obviously a matter for an Egyptologist with medical knowledge, and this was done from a hieroglyphic transcript of the original hieratic writing by Dr. B. Ebbell of Norway in 1936. The meaning of certain words in the language of ancient Egypt is still unknown. There is one word which concerns us particularly. It can best be rendered into English letters as 'a'a. Because of the way in which it is written and the contexts in which it occurs Ebbell and other experts agree that it signifies hæmaturia, indeed no other interpretation is possible, though I personally would suggest that it includes also hæmopermia. The Ebers Papyrus contains twenty prescriptions for the treatment of the malady. Another papyrus, the Berlin Medical Papyrus, contains eleven such prescriptions, and the Hearst Papyrus contains eight. This seems clear evidence that bilharziasis was an important disease in the days of those ancient dynasties. One prescription runs as follows: To expel hæmaturia caused by a god or a dead man in the belly of a man, juice of acacia, juice of pistacia, salt, grapes, honey (and some other items not identifiable) are mixed together and eaten before going to bed.

Ebbell believes that the ancient Egyptians knew that worms caused this disease; he points out that they had opportunities for discovering them during the process of embalming. Among the recipes prescribed for intestinal worms is one which says: "To be eaten by a man in whose belly there are *hereret* worms; it is hæmaturia that creates them; they do not die as the result of any remedy." The worm called *hereret* has not been identified with certainty, yet although cause and effect are transposed, this statement suggests that already in antiquity the Egyptians had observed the schistosomes. Although antimony is alluded to in a composition for dressing for the hair and was also much used for painting the eyes, there is no mention of it as a drug in the treatment of hæmaturia. This is not surprising, as it is of course only effective against bilharziasis when used parenterally.

CLINICAL ASPECTS OF BILHARZIASIS

Post-mortem Examination and Diagnosis.

Dr. Willmore tells me that the easiest way to find the parasite at a post-mortem examination is to incise the portal vein, and to let the blood flow into a flat glass dish, whilst the liver is squeezed. Then dilute the blood with water, rocking it and holding it over a dark surface; in this manner the worms can be seen, resembling minute white threads, usually being curled upon themselves, and, as has been mentioned, they are about the size of the smallest pin. F. M. Sandwith, consulting physician to the Kasr-el-Aini Hospital, Cairo, writing in 1901 reported finding 436 worms in the blood from one liver.

PLATE I
(for acknowledgments see text)



FIG. 2.—Section of male and female worms in copula in the vessels of a retrovesical lymphatic gland. The female on the left side is cut twice and the male appears as if embracing two females. The veins remain open as if arteries. Notice deposition of pigment in all vessels to the point of occlusion.



FIG. 3.—Deposition of eggs by *B. haematobium* in blood-vessels and their passage to exterior. 1, Anterior sucker; 2, posterior sucker; 3, vaginal orifice; 4, uterus with contained eggs.

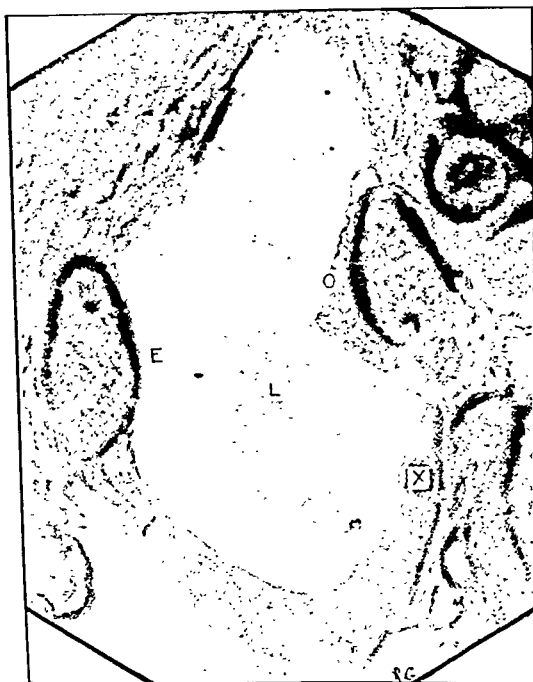


FIG. 4.—Venule of submucosa of bladder, showing an ovum just attached to endothelium by fibrin O, and another midway in endothelium (E). A third one (X) is on the point of leaving the endothelium. L, lumen of vessel. Note that the ova are escaping sideways, the spine playing no part in the process.

omitted when the existence of the disease has been established by the finding of ova in the urine, for it gives a measure of the intensity of the infection, it may reveal important complications and it is a check on the efficacy of treatment. Of course when whole populations of adults and children are affected cystoscopy is not practicable, but during this war it has been used to an extent never hitherto attempted, and with proved value in the treatment of native troops of East Africa. Certainly any urologist practising in this country should make use of it.

Cystoscopic appearances in vesical bilharziasis.—The earliest abnormality seen in the bladder mucosa is the appearance of patches of congestion which occur most commonly in the trigonal region, these, however, have no characteristics which enable certain diagnosis to be made. Subsequent stages are specific and are particularly well illustrated in a paper, "Cystoscopic Appearances of Bilharziasis of the Bladder", by Naguib Makar, F.R.C.S.Eng., Professor of Urology, Faculty of Medicine, Kasr-el-Aini Hospital, Cairo. A selection of these are here reproduced with his kind permission (*see* colour plates).

The first of these stages is very typical. Bilharzial tubercles make their appearance. Each of these is about as large as is the tubercle due to Koch's bacillus, to which it bears some resemblance, that is to say about the size of a pin's head. It is raised above the level of the mucosa and is surrounded by a narrow ring of congested vessels. It has a shining surface and a faintly yellow colour. As it grows and dies the shine diminishes, the yellow colour remains and is sometimes intensified, whilst the surrounding hyperemia becomes less or may disappear entirely. The bladder mucosa which lies around a collection of these tubercles is sometimes congested but maybe very little different from the normal. When an intense invasion by ova is in progress very marked bullous oedema (fig. 22) is often produced. It is difficult to say how much this is a mere reaction to the ova and their toxins, and how much it is due to venous blockage by the worms, but probably the former is the more important cause.

Bilharzial nodules (fig. 11) are larger than tubercles, they are more prominent and greyer in colour, and are more commonly met with in chronically infected bladders. The tubercles may also fuse and give rise to a membrane (fig. 12) which at first has an orange colour, but later becomes grey. The membrane is composed of blood, mucus, epithelial debris and ova. It is very adherent; if detached an erosion is exposed. An area so infected is surrounded by congestion.

These cystoscopic appearances are very characteristic of the disease, and are unlikely to be missed by any experienced urologist, even if he has never before met with a case of vesical bilharziasis.

Some of the later changes are much more difficult to interpret. The examination of a patient with active and advanced lesions is also less easy and it is usually necessary that an anæsthetic be given and a flushing cystoscope employed. In mild and in chronic cases there is, however, one special detail well worthy of the urologist's attention. Sometimes all the fields inspected when looking through the cystoscope in a downward, or in either lateral position, and the region of the bubble are found to be normal. If, however, by a very full depression of the eyepiece the anterior aspect of the bladder be examined, and particularly that part of it which is about half-way between the bubble and the internal meatus, a solitary patch of mucosa affected with bilharziasis may be discovered. Sometimes tubercles are seen here, sometimes only congestion or sandy patches or granulations. This we learnt for ourselves in Egypt where all our cases were Europeans, most of them having been infected in South Africa or Rhodesia, patients who of course reported for examination with symptoms of mild degree. In East Africa also when cystoscopy otherwise healthy native troops who were suspected to have the disease we never omitted to examine this area in detail, that is to say the region of the bubble and the parts anterior to it.

Bilharziasis of the bladder may develop in various ways from these earliest states. The live ova from a tubercle or other infected area of the bladder work their way through the ultimate mucosal covering and are thus shed into the urine, the tubercle then dies a natural death and the healed area leaves no permanent scar. Alternatively dead ova which have not been discharged may remain as tubercles for a long time, but for just how long I do not know (fig. 23).

Calcification of the bladder tissues around the ova is a prominent feature in all severely infected long-standing and untreated cases. In Kasr-el-Aini Hospital, Cairo, X-rays demonstrate calcification in 60% of bladders affected with bilharziasis. It has already been mentioned that the ova when alive are believed to secrete a toxic substance, the function of this being to cause dissolution of the surrounding tissues and thus the release of the ovum into the urine, and it seems very probable that it is this "toxin" which by prolonged action produces the intense sclerosis of the bladder wall, which ultimately goes on to calcification, for it seems unlikely that the ova acting merely as foreign bodies could produce this result.

PLATE I
(for acknowledgments see text)



FIG. 2.—Section of male and female worms in copula in the vessels of a retrovesical lymphatic gland. The female on the left side is cut twice and the male appears as if embracing two females. The veins remain open as if arteries. Notice deposition of pigment in all vessels to the point of occlusion.



FIG. 3.—Deposition of eggs by *B. haematobium* in blood-vessels and their passage to exterior. 1, Anterior sucker; 2, posterior sucker; 3, vaginal orifice; 4, uterus with contained eggs.

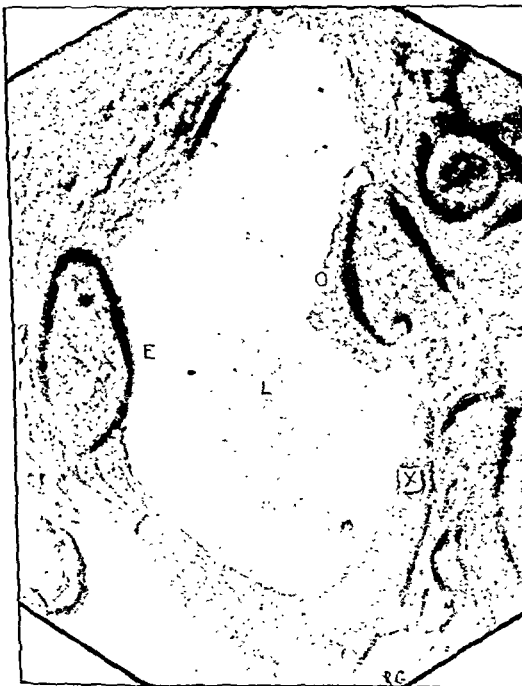


FIG. 4.—Venule of submucosa of bladder, showing an ovum just attached to endothelium by fibrin O, and another midway in endothelium (E). A third one (X) is on the point of leaving the endothelium. L, lumen of vessel. Note that the ova are escaping sideways, the spine playing no part in the process.

PLATE II
(for acknowledgments see text)

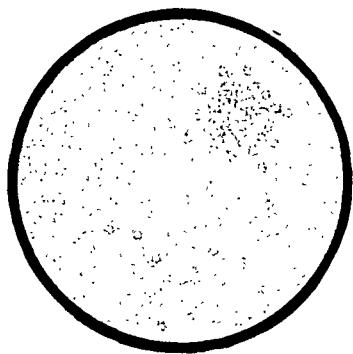


FIG. 10.—Bilharzial granulations or tubercles.

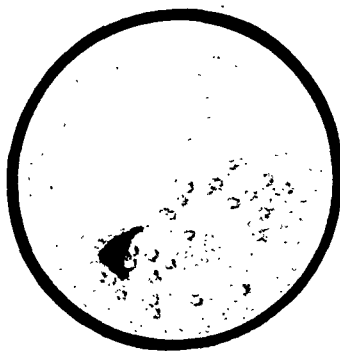


FIG. 11.—Bilharzial nodules. The ureteric orifice is deformed; the surrounding mucous membrane of the bladder is anæmic and has a greyish-yellow colour.

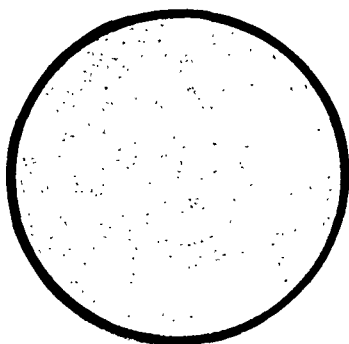


FIG. 12.—Bilharzial tubercles, some of them have fused to form bilharzial membrane which is surrounded by a hyperæmic zone.

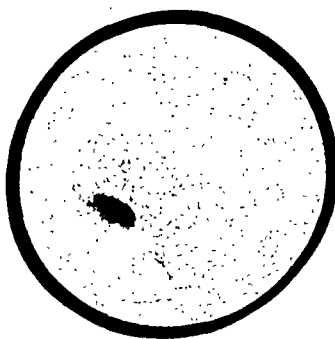


FIG. 13.—Right ureteric orifice with "sandy patches" above it and fused granules forming a membrane below.

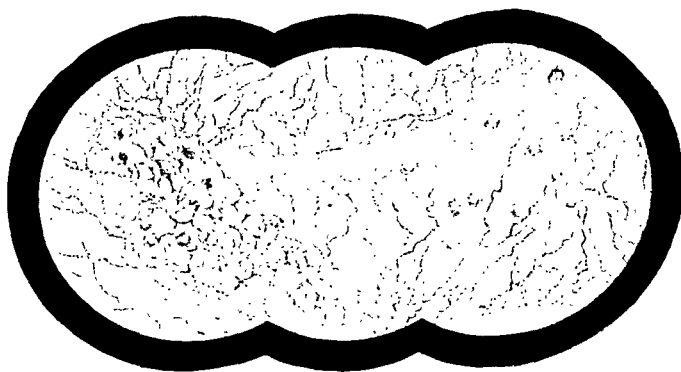


FIG. 22.—Bilharzial disease of the bladder before treatment (see Plate III, fig. 23).

PLATE III
(for acknowledgments see text)



FIG. 14.—To the left of the figure there is a bilharzial ulcer, exposed by the disappearance of a pre-existing membrane. Surrounding it are bilharzial tubercles. To the right an ulcer, well on the way to healing, can be seen in a saccule.

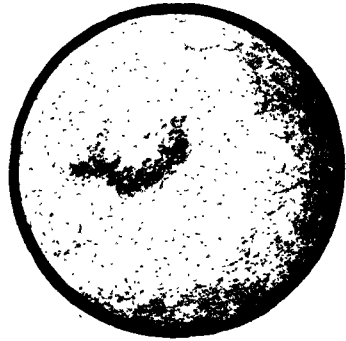


FIG. 15.—Submucous bilharzial mass covered with bilharzial tubercles.



FIG. 16.—On the left is a septic ulcer. On the right is a large submucous mass covered with bilharzial tubercles. The rest of the vesical mucous membrane shows signs of inflammation.

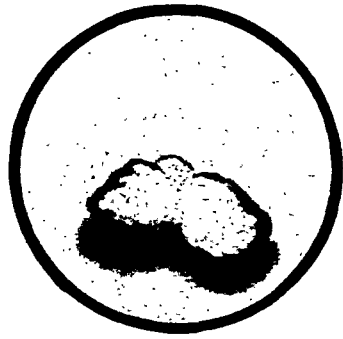
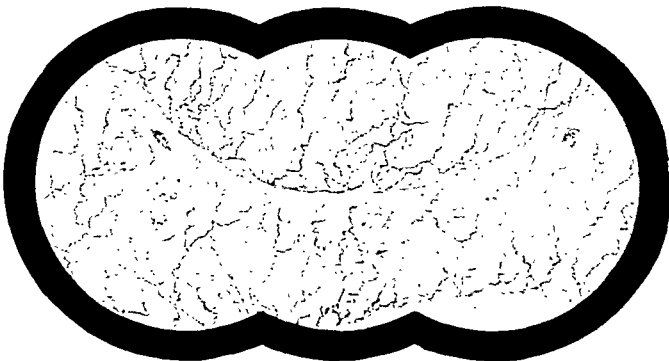


FIG. 17.—Bilharzial papillomata.



W. THORNTON SHIELDS

FIG. 23.—Bilharzial disease of the bladder one month after treatment with sodium antimony tartrate. The yellow nodules are the dead ova working their way through into the bladder cavity. They do not indicate active bilharzial disease. (From *Brit. J. Surg.*, 1934, 21, 632, by permission of the publishers, Messrs. John Wright & Sons, Ltd.)

PLATE II
(for acknowledgments see text)

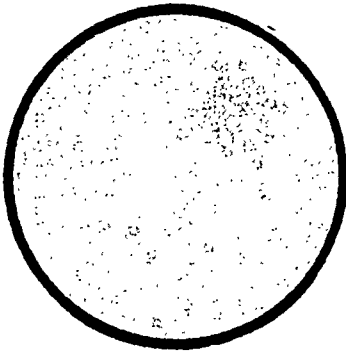


FIG. 10.—Bilharzial granulations or tubercles.

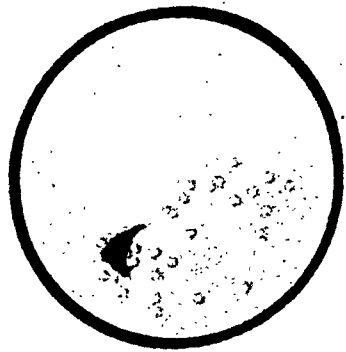


FIG. 11.—Bilharzial nodules. The ureteric orifice is deformed; the surrounding mucous membrane of the bladder is anæmic and has a greyish-yellow colour.

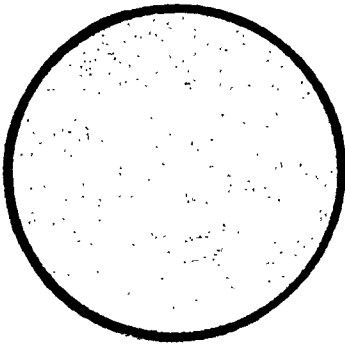


FIG. 12.—Bilharzial tubercles, some of them have fused to form bilharzial membrane which is surrounded by a hyperæmic zone.

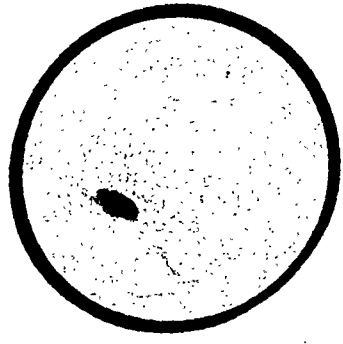


FIG. 13.—Right ureteric orifice with "sandy patches" above it and fused granules forming a membrane below.



FIG. 22.—Bilharzial disease of the bladder before treatment (see Plate III, fig. 23).

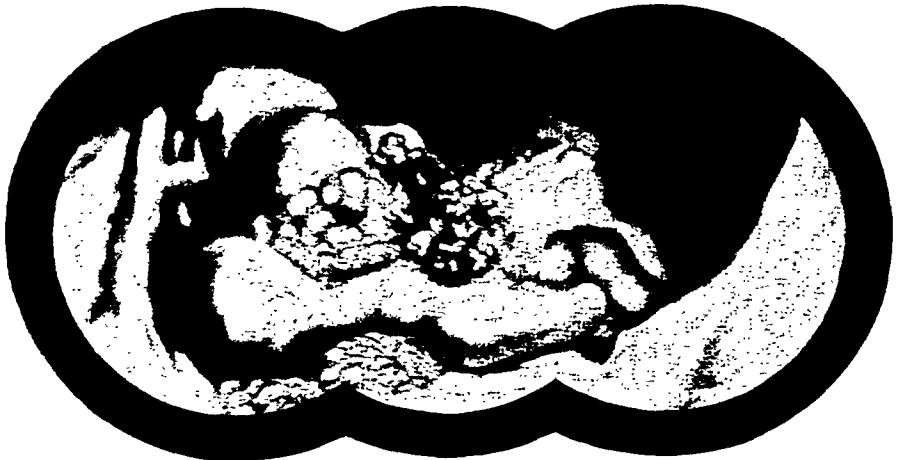
PLATE V

(for acknowledgments see text)



N. Strekalovsky

FIG. 18.—Naked-eye view of malignant papilloma of the bladder (seen through suprapubic wound).



N. Strekalovsky

FIG. 19.—Nodular bilharzial carcinoma of the urinary bladder.

PLATE IV
(for acknowledgments see text)

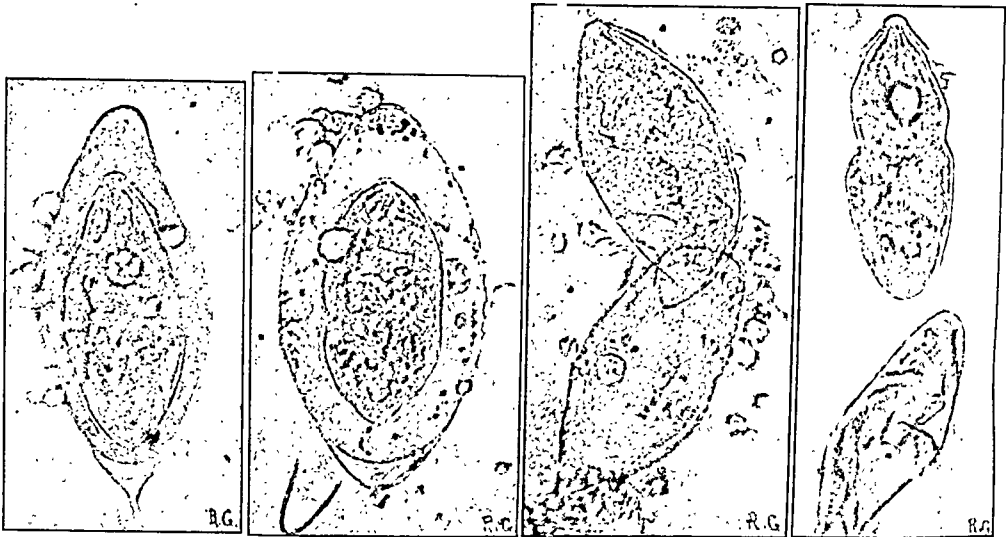


FIG. 6—(a) Ovum imbibing water. (b) Ovum swollen with water just before rupture of shell. (c) Miracidium after hatching. (d) Miracidium leaving shell. Freely swimming.

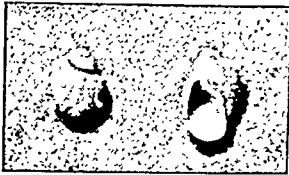


FIG. 7.—*Bullinus contortus* (natural size).



FIG. 8 — Primary sporocyst packed with daughter sporocysts.

S.S. Secondary sporocyst

G.C. Germinal cell.

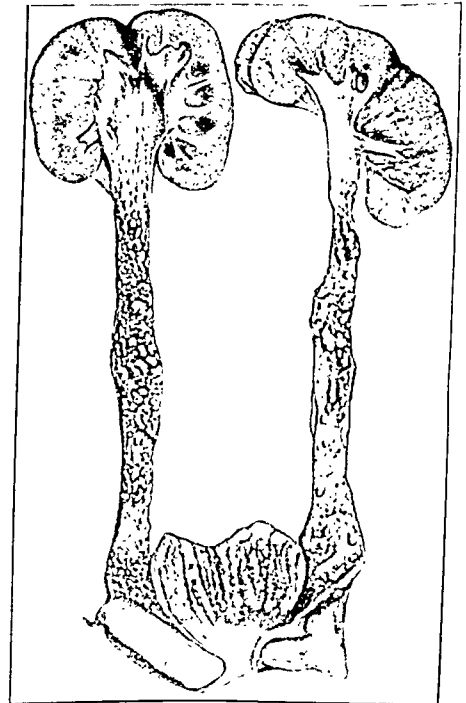
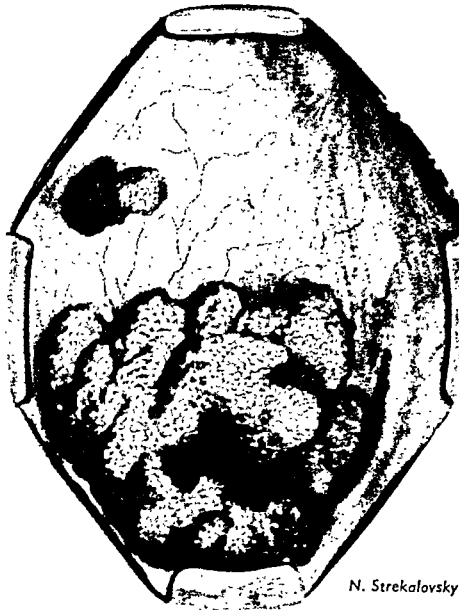


FIG. 20.—Bilharziasis of the urinary tract with formation of papillomata.
(After Morson, *Proc. R. Soc. Med.*, 1937, 30, 152.)

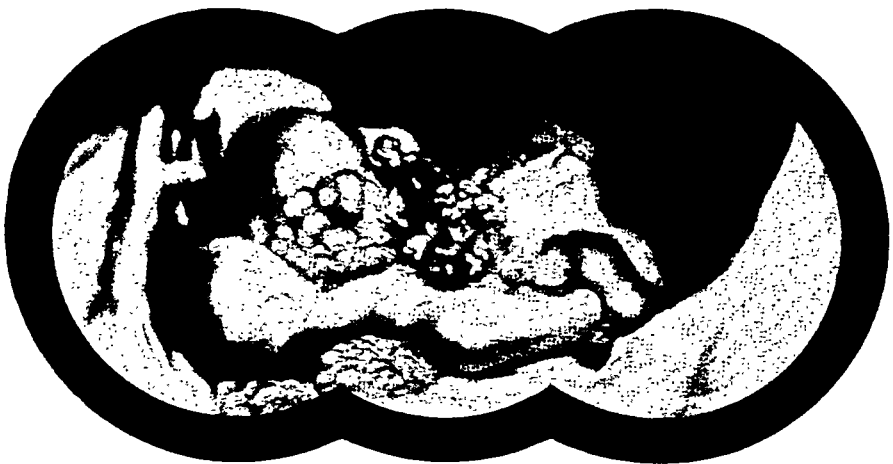
PLATE V

(for acknowledgments see text)



N. Strekalovsky

FIG. 18.—Naked-eye view of malignant papilloma of the bladder (seen through suprapubic wound).



N. Strekalovsky

FIG. 19.—Nodular bilharzial carcinoma of the urinary bladder.

PLATE VI
(for acknowledgments see text)

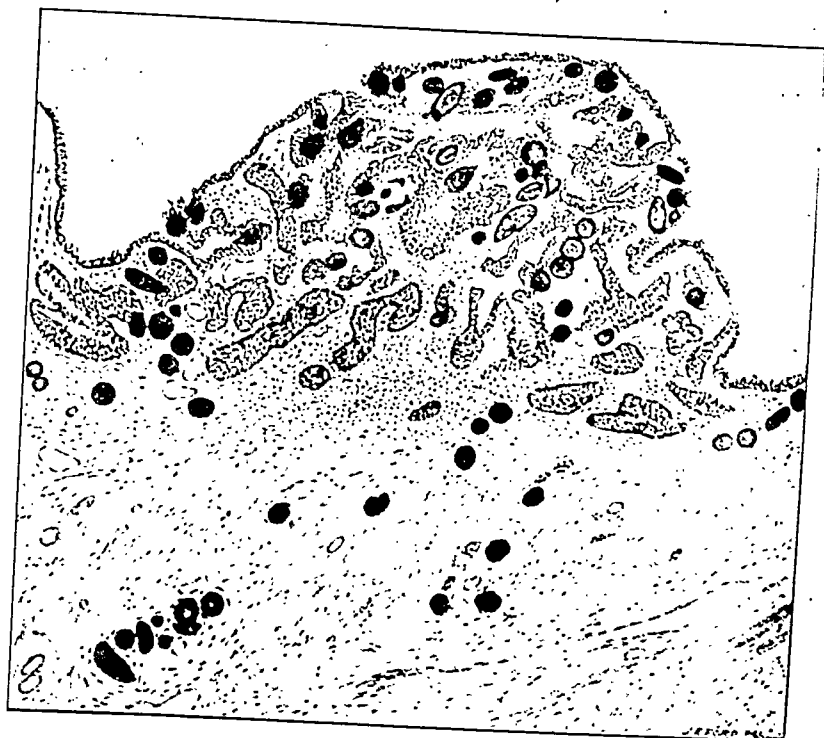


FIG. 5.—Bilharzial tubercle of the bladder wall with ova, some calcified, in the tissues.
(After Ferguson.)

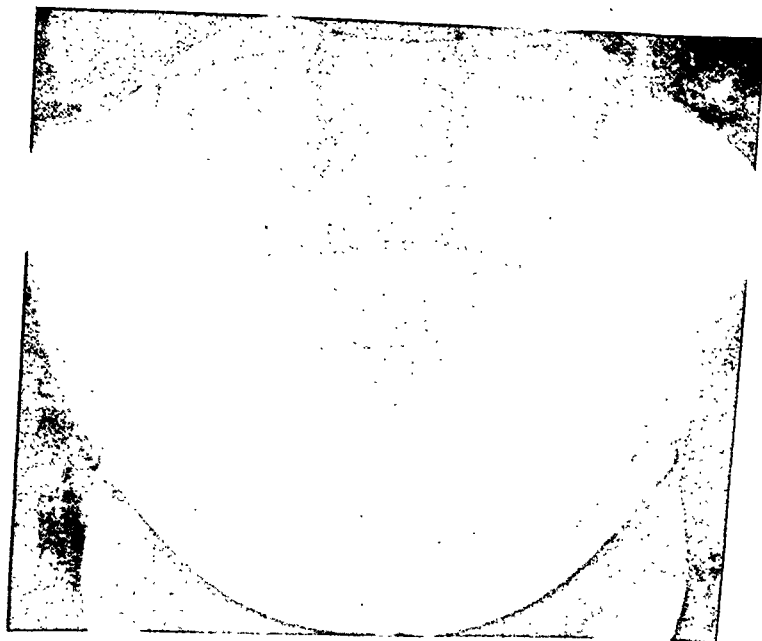


FIG. 21.—Calcification in submucous layer of bladder wall.

One local result of calcification is what is called sandy patches (fig. 13) in the mucosa. Nowadays this term is used to describe characteristic cystoscopic appearances, areas looking like sand under water, produced, as pointed out by F. C. Madden, by aggregations of calcified old tubercles, the epithelium having degenerated. But the name "sandy patch" is much older than the cystoscope, for Dr. Willmore tells me that it was employed to describe the grating felt when cutting through such areas with a knife, or the grittiness elicited with an urethral sound when moved against the trigone and the bladder base. In those early days, though not now, this was a justifiable method of diagnosis, particularly when following such instrumentation it was found that the ova could often be detected in the urine.

The process of calcification affects chiefly the submucous layer of the bladder wall (fig. 21). It is by no means necessarily accompanied by secondary infection, and on cystoscopy in such cases I have often seen the bladder to be clean. If so it is usually very pale owing to sclerosis and diminution of the vessels. This calcification forms a barrier in which many ova perish, and through which others cannot work their way. But though it may break the life-cycle of the parasite, and though it may shield the patient from the pangs of bladder disease, it does not mean that he is cured of his bilharziasis. For if the worms do not die their ova will still continue to attempt to reach the urinary channels, and so do still more damage to the deeper layers of the bladder and to neighbouring tissues. In such cases either cystoscopy or X-ray should make a diagnosis certain, but urine examination will usually fail, for even if the disease is still active and ova are present they cannot necessarily force this barrier. Patients afflicted with the disease in this form often have only symptoms of limited vesical capacity. L. B. Goldschmidt says that such bladders, even when some evidence of calcification is found on X-ray, can often be successfully dilated under spinal anaesthesia. Such treatment would not, of course, be undertaken until antimony had completed its curative effects.

Another stage is the development of a bilharzial ulcer (fig. 14). This may be clean and without sloughs. It is usually single, and Makar says that he has never seen this type of ulcer become malignant. More often secondary infection is co-existent, and in such cases an ulcer, also usually a solitary one, has a sloughing base and marked cystitis is present.

Secondary infection is very common in Egypt, but is much less often met with in East Africa. In its worst form it leads to a degree of cystitis more severe than in any other disease. The bladder becomes intensely contracted and filled with blood-stained, sloughing, oedematous and shaggy masses of mucosa which resemble a secondarily infected carcinoma, from which it may be very difficult to distinguish.

When large numbers of the ova collect in the submucous layer they may cause tumour-like bilharzial masses (figs. 15 and 16) to project into the bladder. These are composed of fibrous granulation tissue packed with eggs. Tubercles are often seen on the surface of these masses, from which ova are commonly shed in plenty. Such masses are not neoplasms and must be distinguished from them. This condition can be cured by anti-bilharzial treatment. That the distinction is not always easy may be illustrated by a story of a urologist of this country who was about to perform partial cystectomy for carcinoma upon an Egyptian when a cable from relations in the patient's home town requested examination of the urine for bilharzia. This A. H. Harkness was asked to undertake, he did so, found the ova, and later dispersed the tumour with antimony.

Vesical papillomata (fig. 17) due to bilharzia are common in Egypt. This is a true neoplastic condition and frequently malignant. In that country cancer of other organs is uncommon, and these growths are considered to be the result of the "toxins" of the ova. In two years at the Kasr-el-Aini Hospital out of 130 cases of carcinoma of the bladder 114 were of the papilliferous type, and the great majority of these were judged to be the result of bilharzial disease. Twenty-two occurred in patients under 30 years, fifty-seven in patients between 30 and 40 years. One hundred and seventeen were males, thirteen were females. One hundred and ten occurred in field labourers. Makar says, however, that bilharzial cancer is also not rare in the upper classes of Egypt. A bilharzial papilloma, unlike a granulomatous mass with which it sometimes may be confused, is of course not to be cured by medical treatment. These growths do not have long fronds but are of firm consistency (fig. 18). Usually there are only two or three of them. The commonest variety of bilharzial papilloma met with in Egypt is of bulbar form and dark red colour though in parts it has a greyish-white appearance due to septic necrosis and to phosphatic deposit in the growth. These growths may spread and in rare cases involve the greater part of the bladder. Nodular infiltrating carcinomata (fig. 19) are less common. In the series of one hundred and thirty cases and follows the course common to all bladder carcinoma of this type.

PLATE VI
(for acknowledgments see text)



FIG. 5.—Bilharzial tubercle of the bladder wall with ova, some calcified, in the tissues.
(After Ferguson.)

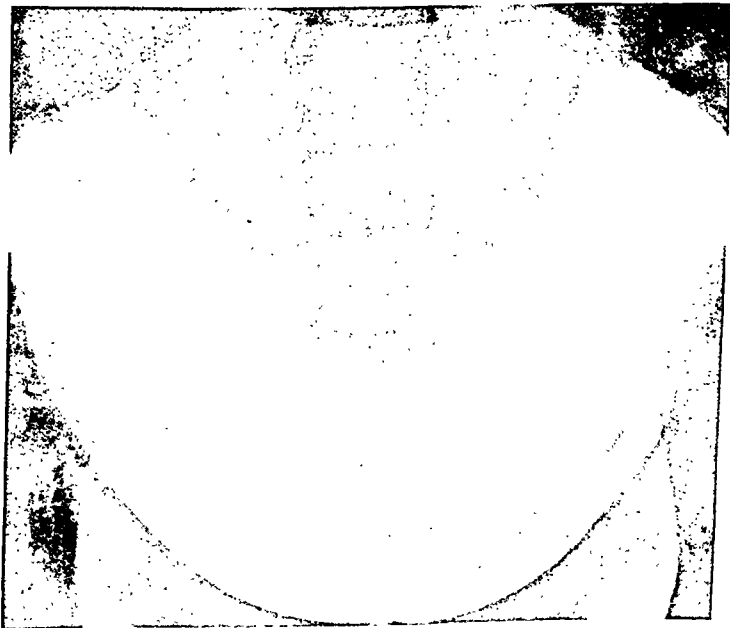


FIG. 21.—Calcification in submucous layer of bladder wall.

Radiography is a useful aid to diagnosis in this condition. X-rays of the pelvis may show, as has been said, calcification throughout the wall of the bladder, often only as a fine line of opacity (fig. 21), but this is not necessarily present. Calcification may also be seen in the lower ureters. Excretion X-ray urography, however, shows the lower parts of the ureters to be dilated and the strictures to be either at the entrance to the bladder, or one or two inches above that part. In later stages the ureters may be dilated throughout their lengths and hydronephrosis may be present, these are sometimes of severe degree. The best method of diagnosis when a stricture is suspected is the passage of a bulb-ended ureteric bougie, for this will prove conclusively its presence or its absence.

TREATMENT OF STRICTURES OF THE URETER

Dilatation of an established stricture of the ureter is best effected through an instrument of the McCarthy panendoscope type, using some form of stiff ureteric dilator. Such methods when possible are very effective, more so it seems to me than in any other types of ureteric strictures, and though the case requires further supervision the cure is often complete. L. B. Goldschmidt confirms this opinion and says that he has only thrice found it necessary to open the bladder in order to treat resistant strictures. But such conditions do exist and will obviously occur most frequently in territories in which the disease is specially prevalent, and when no bougie can be passed treatment is, of course, more difficult. I am indebted to Mr. H. Currie Brayshaw of Johannesburg for an account of the operative technique to be employed in certain selected cases:

"In bad strictures one can occasionally do a meatotomy using a Collin's electrode, but often the strictures are higher up and one has to rely on dilatation. In these cases where even the finest filiform bougie cannot be passed, or where the ureteric orifice cannot be found despite indigo carmine, then open operation is resorted to. The ureters are exposed extraperitoneally through a mid-line incision, and the bladder is also opened. The dilated ureter is incised above the stricture and attempts are made to pass a filiform guide, and if successful a gum-elastic bougie is next passed. Then from the intravesical aspect an incision is made through the mucosa of the ureteric orifice on to the bougie, thus splitting the ureteric opening wide open. Larger bougies are then passed. A stitch is now put on either side through the cut made in the ureteric orifice. A small rubber tube (14 French catheter gauge) with numerous side holes is then passed up the ureter to the renal pelvis and a retaining stitch of catgut is inserted through the mucosa at the ureteric orifice, which also picks up the rubber tube. The extraperitoneal incision in the upper part of the ureter is stitched with continuous catgut, a de Pezzer tube inserted into the bladder, and this with the lower portions of the two ureteric tubes is brought out through the abdominal wall. Drains of soft rubber are placed down to each ureter where they were incised and into the cave of Retzius. In cases where the filiform bougie cannot be passed through the stricture into the bladder, a 3/5 English metal bougie is passed down to the stricture, and where this is caused to project under the mucosa of the bladder an incision is made on to it and the bougie is then forced into the bladder. The remainder of the operation then follows the course already described. If the strictures are several centimetres above the bladder, the ureter may have to be divided and transplanted into the bladder (using the cuff technique of Van der Veen)."

TREATMENT

I do not propose to discuss the general treatment of urinary bilharziasis, or of the later complications of the disease. Until treatment with antimony sodium tartrate was introduced by McDonagh (1912) and Christopherson in 1917 there was no known cure for the disease, and therefore no hope for the 90% of the fellahin who were infected. Filix mas was employed without effect except sometimes to cause blindness, for it often was used in conjunction with castor oil in which it is very soluble, and thus it produced a degeneration of the retinal vessels. Thymol was also tried but without availing anything. Bladder washes with solutions of quassia occasionally liberated worms, and sometimes appeared to relieve symptoms. Surgical relief of urethral obstruction was often required, also operations for calculus, clot retention and severe degrees of contracted bladder. Frequently this was all that could be done for the patient. Dr. Willmore tells me that he has performed Cock's perineal puncture in hundreds of cases, the bladder being too contracted to admit of suprapubic approach. Since those days much has been done in Egypt to cure the disease, particularly by treating the school children, and many attempts have been made to eliminate it. Of the latter the most important is the periodic closing of the irrigation canals, the mud is then dug out and allowed to dry on the banks under the sun, a process which kills the snails.

Tartar emetic remains the best drug, despite some unpleasant effects experienced by the patient during the period of administration. The course should amount to a total of 30 grains, and it must be intensive lest the parasites acquire a resistance to antimony. There are also some more recent preparations such as stibophenum, anthiontaline and fowadin. These are administered intramuscularly, and this is of great value in the

Amongst the primitive population of the Nile Delta these malignant growths often produce great extensions and also widespread metastases before the patient reaches the hospital, and in such cases the symptoms of pain, strangury, frequency and bleeding attain most severe degrees. Sarcoma is rare, but Ferguson found six instances amongst two hundred and forty post-mortem cases of vesical bilharziasis.

URINARY OBSTRUCTION AND FISTULÆ

In untreated cases the musculature of the bladder which is the seat of this disease tends to be thickened, partly owing to hypertrophy and partly because of fibrosis by the additional development of prostatic and urethral obstruction, resulting from bilharzial changes in those tissues. Despite such obstruction the bladder in these cases often remains contracted, and if so this renders suprapubic cystotomy very difficult or impossible to perform. To-day the most advanced degrees of obstruction are probably less common in Egypt than they were in the days before antimony was used as a cure. So also are urinary fistulæ which are a direct result of the disease. These affect all parts, but particularly the floor of the urethral bulb, and are often so numerous and extensive that when the male patient squats to micturate the perineal effect resembles the spraying from the rose of a watering-can. These fistulæ sometimes track widely. Willmore once saw one patient who could micturate only through an opening at antero-internal aspect of the knee. In 1901 Sandwith found that 14% of the bilharzia cases in the Cairo hospital suffered from fistulæ of the bladder or urethra. Ova are often found in the fistulous tracks.

Vesical calculi are met with in bilharziasis and the ova have been in rare cases found within the stones, for example Goebel found certain ova in 8 out of 68 calculi. In 1901 Sandwith reported 14% of bilharzial cases at the Kasr-el-Aini had calculi, more recent reports give a lower percentage. These calculi appear to be composed of uric acid and oxalates, and are formed upon debris. Phosphatic calculi are very common when sepsis has become severe. Renal calculi are also met with, though they are very much less frequent. It is of interest that Elliot Smith, who with Wood-Jones examined, or studied records of about 30,000 mummies, found only two examples of vesical calculus and three of renal calculi. This may be interpreted to mean that modern methods of irrigation in the Nile Delta have greatly increased the incidence of the disease; I think a more probable though partial explanation is that only the bodies of the upper classes were embalmed, and these personages ran much less risk of infection than the labourers in the fields. Nevertheless the discrepancy is very remarkable. Shattock failed to find ova in two of these calculi despite laborious research.

Death amongst the fellahin affected with this disease who have not been effectively treated is due to extreme suffering resulting from bladders secondarily infected, to uræmic sepsis, or to malignant disease. In East Africa such conditions are rarely met with, probably because the infection is much less severe.

OBSTRUCTION OF THE URETERS

Ureteric obstruction of moderate degree is often met with during the active stage of the disease. In such cases it will disappear when a course of treatment with antimony has had time to kill the worms and thus cause the acute reactive processes to resolve. As a result of this the usual symptoms of aching pain in the loin or colics are relieved.

Chronic ureteric stricture is a very important and frequently insidious result of bilharziasis and one which we must be prepared to diagnose and to treat. It affects the lower parts of the duct, for the upper portions lie in an area which is but rarely invaded by the worms. Most of the various pathological conditions which arise in the vesical mucosa may also be met with in the ureters (fig. 20), but stenosis is the common complication and though it may sink into relative insignificance in the clinical picture of a native affected by advanced urinary bilharziasis, yet in such patients death from infected bilateral hydronephrosis is common. These strictures, however, are met with in patients who appear at first sight to have recovered completely from the disease. I have had experience of a good many of such cases. The patient may have no bladder symptoms, he may or may not have suffered from renal colic, ova may not be found in the urine, and on cystoscopy there may be no active bilharzial lesions. Typically in such cases the vesical mucosa is unduly pale and very few vessels, sometimes none, are to be seen; the surface may be smooth or it may be slightly roughened, fasciculations and sandy patches may be present, but often there are none. The ureteric orifices at this stage are often not inflamed but they are rigid and they look lifeless, they are not retracted and do not resemble the dark golf-hole ureter of renal tuberculosis.

Section of the History of Medicine

President—Sir ARTHUR MACNALT, K.C.B., M.D.

[November 1, 1944]

The Medical Career of Jean-Paul Marat.

By H. P. BAYON, M.D.

THE "Friend of the People" has been considered an eminent physician or a low-down quack, according to whether the writer admires or condemns Marat's political activities from 1790 to 1793; for it was only then that he became known as the "tiger that would have drunk the blood of his mother from the skull of his father". Previous to these revolutionary years, Jean-Paul was a whole-hearted admirer of Jean Jacques Rousseau (1715-78) that is, a mild humanitarian—in theory. To obtain a complete picture, reference must be made to Marat's works on heat, light and electricity, since he was a keen scientific experimenter during most of his life.

Existing documentation provides a clear impression of "Dr. Marat's" qualifications and practice, so that his significance in relation to medical and scientific progress can be ascertained.

BIOGRAPHICAL NOTES

His father, Giovanni Mara of Cagliari, Sardinia, was an artist or designer and teacher of languages; he married Louise Cabrol of Geneva, the daughter of a wig-maker; these occupations explain some obscure periods in Marat's life, for it has been suggested that at one time he taught "tambouring", i.e. designs for embroidery, and that he had been a hairdresser.

Jean-Paul Marat was born at Boudry, Neuchâtel, May 24, 1743, and at the age of 16 left home to become tutor to a family in Bordeaux; it was probably then that he added a "t" to his name, so as to Frenchify it. He left two years afterwards and it is uncertain what he did or how he lived till he came to London some time in 1766-67; for this we have evidence from Farington's Diary—December 6, 1793—where it is recorded that Marat lodged in St. Martin's Lane and said that he was in England to complete his studies; that he was friendly with Antonio Pietro Zucchi (1726-95)—who later married Angelica Kauffmann—and borrowed £500 from him; medically cured and treated Joseph Bonomi (1759-1808). Where Marat obtained his medical knowledge is unknown; it can be assumed that he was an autodidact by books. Farington mentioned that an apothecary told him that Marat did not conform to common usage in his prescriptions.

After five years residence in Great Britain his first work was published anonymously: *An Essay on the Human Soul* (1772), in this he quoted Albrecht von Haller (1708-77), whom he may have met and several other authorities that were dead—like Boerhaave (1668-1738), Théophile Bonet (1620-80). In this essay, Marat suggested that there were seven senses; to the usual five he added hunger and thirst; he said that nerves carried two fluids, one sensory and the other motor; his evidence was that when a nerve was tied, sensation and motility ceased; he placed the soul in the meningeal membranes. Modern concepts of the soul differ from those of his time, but it is known that by peeling off the *pia mater* the higher faculties of the brain may be impaired; this is, however, due to the resulting lesions to the small blood-vessels and the concurrent circulatory disturbances.

It was in 1811 that Sir Charles Bell (1774-1842) separated the functions of the roots of the spinal nerves and even then, clearly visualizing the function of the anterior roots alone. He completed his discoveries later, recording them in his book on the nervous system in 1830; but meanwhile, in 1822, Francis Magendie (1785-1855) had published experimental proof of the separate different functions of the nerves.

treatment of the school children of the Delta. They obviously have advantages when large numbers of troops have to be treated but they are not considered to be so certainly curative as is antimony sodium tartrate. Antimony first sterilizes the generative apparatus of the female worms and ultimately destroys them. It is not known just how certain is the effect upon those ova which have been deposited before treatment was begun.

My only case of bilharziasis in pre-war years was a young man, aged 20, who was infected after spending just over one year in a place about 70 miles distant from Salisbury, the capital of Southern Rhodesia. This is a country where bilharzia is well known yet his fever, hæmaturia with the passage of clots of blood, and once an unexplained attack of retention of urine for thirty-six hours, had remained undiagnosed. He came to see me when he returned to England. I sent his urine to Dr. Cuthbert Dukes, and he found the ova. When I cystoscoped him the appearances were typical (figs. 22 and 23). He was treated by Dr. J. B. Christopherson who cured him with tartar emetic.

It will be agreed that we must keep our eyes open for occasional cases of this disease. Not only have officers and men of all three Services served in countries where this disease is endemic, but there also are to be remembered the children of those of our people who at all times follow their occupations in these territories. It is not only the unalluring channels of the Sweet Water Canal which harbour the disease.

A doctor friend of mine, who was brought up in Pietermaritzburg, Natal, tells me that he was educated there in a school of 600 boys, they all bathed in the neighbouring river, and 70% of them had terminal hæmaturia. He himself suffered from this all the time he was a medical student and during the last war, with occasional attacks of renal colic, which were followed by the passage of a clot or a small oxalate stone. He was one of the first cases to be cured by Christopherson with antimony.

Egypt, the territories of the Union of South Africa, and East Africa are all places where the British race makes its home, and in all the disease may be acquired though the Highlands of Kenya are relatively immune. Therefore a history of service in any of these places may be important when bladder disease is being investigated. Urologists must, therefore, know how to diagnose the early stages of bilharziasis, whilst its later manifestations will remain chiefly a matter of general interest. Failure to demonstrate the ova in the urine, particularly in a solitary specimen, does not exclude the disease. Cystoscopy takes a high place in diagnosis in every stage of the disease, and is of great importance in the control of treatment. The insidious danger of ureteric obstruction occurring when all signs of active parasitic infection have faded from the scene must not be forgotten. Moreover we must be aware of the fact that the worms, when their normal vein paths are obstructed, may find their way to the seminal vesicles causing hæmospermia, also to the prostate (Goldschmidt has found ova in tissues removed by prostatic resection), vas, epididymis, testis and tunica vaginalis, and produce sclerosing or infiltrative changes in these organs. Finally we must not forget that a patient who has become infected with *B. hæmatobia* may well have become invaded by *B. mansoni* at the same time.

ACKNOWLEDGMENTS

Special thanks are due to Dr. Naguib Makar, F.R.C.S. Eng., Professor of Urology of the Faculty of Medicine, Cairo, for the loan of the paintings for figs. 10 to 17 which illustrated his paper on bilharziasis of the bladder in the *Journal of the Egyptian Medical Association*, 1932, and for figs. 18 and 19 which appeared in "A Preliminary Note on Bilharzial Cancer of the Bladder", published by the Ministry of Public Health, Egypt, 1938. Figs. 5 and 21 also appeared in this publication.

Figs. 1, 2, 4, 6 and 8 are reproduced from "Schistosomiasis", by Rameses Girges, by kind permission of the publishers, Messrs. John Bale Medical Publications Limited. Figs. 3 and 7 are from "Manson's Tropical Diseases" by courtesy of Sir Philip Manson-Bahr and Messrs. Cassell & Co., who have also kindly lent the colour blocks for figs. 22 and 23.

and seemingly obtained considerable improvement. In the third patient Marat mentioned "a scorbutic habit" which was cured by "anti-scorbutic Remedies" such as water-cresses, bitter plants, &c. In both tracts there is no lasting contribution to the pathology or therapy of the diseases treated; it is quite believable that by persistent care and attention, Marat did obtain a definite measure of success in these cases. What is most remarkable is that no one would recognize in the obsequious, candid style of these communications, the hand of the bloodthirsty Deputy of *La Montagne* in the Convention of Paris.

Phipson in 1924 ascertained that Marat was not a householder in Church Street, Soho; the prefaces of the two tracts having been dated from there is no evidence whatever that Marat carried on a flourishing medical practice from that address, nor are the dates any proof that Marat was there at the time.

It was at this time that a remarkable incident occurred in Marat's life, no less than a theft from the Ashmolean Museum, Oxford, and his conviction to the hulks at Woolwich. All this has been denied by the majority of his biographers, but the clear evidence available will be quoted elsewhere in the near future.

What is relevant to Marat's medical career is that in May 1777 he was in Paris and called to treat the Marquise de Laubespine, who was suffering from phthisis, as a physician *lately* arrived from England.

A few words may be said about Mme de Laubespine, whose case is described by Cabanès, "*Marat Inconnu*" Paris, in Chapter VIII entitled: *Marat et les femmes*; but here we prefer to examine her case as one of pulmonary tuberculosis. That she really suffered from the disease can be accepted; five years before she had developed a dry cough, shortly after a confinement; this may well have been the flaring-up of a cryptic infection following pregnancy—a not uncommon occurrence. Notwithstanding treatment, the disease progressed, the patient lost weight, expectoration became purulent. When Marat undertook treatment, he prescribed an emulsion of almonds with salts of nitre, to which he added a secret remedy, which subsequent analysis showed to be an artificial mineral water, similar to that of Harrogate. Then followed laxatives in the shape of "*Sels de policreste*"; further, quinine extracts and Peru balsam, together with fifty drops of ambergris in a cup of cow's milk every morning. Marat does not appear to have performed percussion or auscultation, though Leopold Auenbrugger's (1722-1809) book *Inventum novum* had appeared in 1761 and had been translated into French by Rosière de la Chassagne in 1770. This useful diagnostic method had to be revived in 1808 by Jean-Nicholas Corvisart (1755-1821).

In any case in June and July of 1777 the Marquise was considered to be cured; four years afterwards she was still alive, but her subsequent life-history is unknown; her sudden improvement may well have been due to one of those remissions with temporary relief that occur in tuberculosis of the lungs. Whatever the explanation may have been, Marat's success was skilfully advertised in the *Gazette de Santé* in an article by the Abbé Fillassier [? Jacques Joseph Fillassier (1745-99) author and great admirer of Rousseau]. Unfavourable critics also wrote to the *Gazette* and the Marquis de Laubespine replied, defending Marat, who also took part in the debate in December 1777.

It was Mme de Laubespine who recommended Marat to the Comte d'Artois, who then appointed Jean-Paul Marat, "a Doctor of medicine of several faculties in England" as *Médecin du Corps des Gardes* with a brevet dated June 24, 1777—which Cabanès reproduced in facsimile—pp. 104-5.

In consequence of all this, Marat was approached by several patients and entered into correspondence with others outside Paris: soon after Marat was living in an elegant apartment in the Faubourg St. Germain; his practice may well have been extensive and lucrative. How long this prosperity lasted can be approximately ascertained, because by 1783 he was trying very hard to obtain the position as head of a newly formed academy in Madrid and showed a great interest in all things Spanish. He said that his practice had suffered as the result of professional jealousy and slanders—that medicine gave him no satisfaction, when compared with the pursuit of scientific aims. He was not accepted for this post, because some French Académicians spoke and wrote against him; this is quite believable.

Next year Marat's last medical writing was published: *Mémoire sur l'électricité médicale. Couronné le 6. Août 1783, par l'Académie Royale des Sciences, Belles Lettres & Arts de Rouen* (Paris, 1784), Jorry. This is probably the best piece of work Marat did; it is mainly concerned with contesting the effects of electricity on various diseases; on p. 2 he mentioned: "... des prétendus miracles opérés par les mains des Pivati, des Verrati, des Brigoti, des Bianchi, &c." Much is also said about Abbé Bertholon, who had stated that fever was due to an excess of electricity in the blood. This was Pierre Bertholon (1742-1800) author of: *De l'électricité du corps humain dans l'état de santé et de maladie. Ouvrage couronné par l'Académie de Lyon*. Two vols. (Paris,

Most biographies of Marat—and there are many—mention that he sent one of his works to Professor Collignon of Cambridge, who wrote praising the book. I have traced Charles Collignon (1725-85), M.D., F.R.S., professor of anatomy, author of: *An Enquiry into the Structure of the Human Body Relative to its Supposed Influence on the Morals of Mankind* (Cambridge, Second Edition, 1764-65), Bentham. *Medicina Politica or Reflections on the Art of Physic as Inseparably Connected with the Prosperity of a State* (Cambridge, 1765), Bentham.

Collignon wrote to Marat on May 1, 1773, a somewhat thin-lipped acknowledgment of the *Essay on the Human Soul* which Marat translated and added to his letter to Philippe-Rose Roume de St. Laurent in 1783. It should be noted that Vellay (1908), p. 49, gives the reference of Collignon to a "somewhat lively description" as occurring on page 857—it obviously should be page 257, Vol. I of the *Essay*.

In Vellay (1908), p. 12, there is the translation of a letter of Marat to a Mr. William Daly, dated from Paris, "December" no year. From the fact that Marat begged to be excused for his faulty English it can be surmised that it was written in the first years of his residence in Great Britain. In it, Marat said that his heart was "as tender as yours"; then explained why he anatomized animals for medical and surgical purposes; that he foresaw the time when experiments on animals would be as universally adopted in France as in England; that he could obtain many cadavers and announced the early appearance next year of his work. He invited Mr. Daly to come and study with him in Paris. At this time (? 1770) it is more than probable that he tried to obtain the acquaintance of John (1728-93) or William Hunter (1718-83) who in 1768 had built the Museum in Great Windmill Street.

So far there is no evidence that Marat was established as a regular medical practitioner in London, but it can be accepted that he practised human and veterinary medicine in Newcastle some time between 1772 and 1774.

The same year Marat went to Holland and, on his way back, stayed in Edinburgh during June and August 1775; it was then that he obtained the degree of M.D. from the University of St. Andrews on the strength of being an *Artium magister*—which seems to have been a bit of wishful thinking; it was of this University that Dr. Samuel Johnson remarked that it had become wealthy by degrees.

Then Marat's first medical tract made its appearance: *An Essay on Gleets. The Defects of the Actual Method of Treating Those Complaints of the Urethra are Pointed Out, and an Effectual Way of Curing Them Indicated* (London; printed for W. Nicoll—no date). This was dedicated from Church Street, Soho, November 21, 1775, to the Worshipful Company of Surgeons in London. The two known copies are in the Library of the Wellcome Research Institution, London. In a footnote on the first page, Marat stated that if his essay should meet with approbation, he would offer to the public a new method of radically curing gonorrhœa in a short time!

In the text Marat described the treatment of three cases of chronic urethritis by means of suitable *bougies*, a method introduced by the Frenchman Jacques Daran (1701-84); one of Marat's patients had been unsuccessfully treated by Daran. Marat's treatment consisted in employing different *bougies* according to the stage of the infection; this seems to be an improvement on Daran's method.

The next tract was: *An Enquiry into the Nature, Cause and Cure of a Singular Disease of the Eyes, Hitherto Unknown, and Yet Common, Produced by the Use of Certain Mercurial Preparations* (London; printed for W. Nicoll—no date). This was addressed to the Royal Society, from Church Street, Soho, January 1, 1776; but its Library does not possess a copy. The only known exemplar is in the Royal Society of Medicine, London; it was discovered by the late Sir John Macalister (1856-1925) in a bundle of tracts forgotten in a basement.

In the text Marat described the treatment of three cases of inflammation of the eyes, in patients having undergone mercurial treatment and said that the condition had been confused with *gutta serena*, a term which implied failing eyesight or approaching blindness, in contrast to *gutta opaca*, or cataract with blurred vision; a medical wit said that *gutta serena* was the ailment when neither physician nor patient could see clearly. In Marat's case this diagnosis had been made by "a Fryar of some repute for curing Diseases of the Eyes". The connexion between mercurial treatment and this ophthalmia cannot be established and Marat's description of the symptoms does not allow one to recognize more than the swelling of the ocular muscles, which might influence the curvature of the lens—thus involving lack of accommodation. Marat did not know this function of the lens, though it had been mentioned in Descartes' *Dioptrica* (1637) but even Thomas Young (1773-1829) in 1792 did not give a complete description of the mechanism of accommodation.

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1786), Croulbois. Bertholon was a friend of Franklin and member of numerous academies; all the same, his medical observations are obviously superficial; moreover he had suggested preventing earthquakes by planting deep lightning conductors into the earth.

Garrison (1929), p. 327, said that electro-physiology had its origin in the epoch-making experiments on muscle-nerve preparations summarized by Luigi Galvani (1737-98) in: *De viribus electricitatis in motu musculari* (Modena, 1792). John Hunter had studied animal electricity in the torpedo fish (1773); which had been used in therapy by the Romans; Cالدani had already experimented on electrical stimulation of the cerebral cortex (1784), but Galvani's discovery of the properties of excised tissues is the starting point of modern work. On the next page Garrison wrote: "Meanwhile Benjamin Franklin (1706-90), Kratzenstein (1745), Schaeffer (1752), G. F. Roessler (electric bath, 1768), Mauduyt (1777), William Henly (1779), and many others were already utilizing electricity in the treatment of disease. Static machines were installed in the Middlessex Hospital in 1767, &c." It is therefore quite evident that Marat did not introduce therapeutic electricity, but rather denied the claims being made by others, though he reported employing electrical sparking with success in his tract on "Eyes". In this *mémoire*, Marat mentioned that in 1782 he had noted a slight improvement in the chilblains of three boys treated with electric sparks. He also referred to experiments on animals performed in October 1781 and March 1782. His conclusion was that treatment by electrical sparks or friction was useless in many diseases and in some—such as cancer or epilepsy—might even be harmful, if too violent.

Marat was dealing with a subject that was in its earliest stages and it is difficult to understand Cabanès (1911) who suggested that Marat had foreseen the use of X-rays. Such fantastic assertions are quite common in biographies of Marat.

Early in 1784 the appointment with the Count of Artois was ended, though as the result of an oversight, Marat's name continued to appear in the household list till his successor, Dr. Enguehard of Montpellier, entered the post on April 23, 1786.

This position was both lucrative and dignified; one of the physicians in the same household was Félix Vicq d'Azyr (1748-94) a renowned comparative anatomist. There was a separate veterinarian for the stables.

Once more it becomes difficult to follow Marat's movements or ascertain his means of livelihood; it has been suggested that he returned to England, opened a bookshop in Bristol and failed, being then imprisoned for debt in the name of Marat Amiat; if so he was released in December 1787 and in January 1788 was again in Paris. The evidence for the Bristol incident is contradictory but in 1788 the last scientific work of Marat was printed.

A few words will suffice for Marat's investigations of the phenomena of nervous impulses, light, fire, electricity. It has been seen that he propounded that nerves acted through a fluid with dual properties; later on he became obsessed with the theory that fire was a fluid and proved it by means of the so-called solar microscope or lenses combined with a *camera obscura*; the appearance of hot gases was so similar to that of flowing liquids; even Phlogiston was also a fluid! He then attacked Newton in relation to his observations on light; Marat held there were only three primary colours—red, blue, yellow. Electricity was also a fluid: lightning conductors were useless—here he fell foul of Benjamin Franklin. Marat accused Lavoisier of plagiarism in relation to Cavendish; some of Marat's admirers have written that he attacked Lavoisier as a *Fermier général*, not as a scientist; this is an absurd misstatement; one need only read: *Les charlatans modernes* (1791). Imprimerie Marat.

Not all contemporary notabilities ignored or opposed Marat—Lamarck and Goethe quoted him with approval.

From June 1789 onwards, Marat's activities are relatively well documented; Carlyle was wrong in saying that Marat took part in the attack on the Bastille. Marat soon developed into a fervid revolutionary journalist, voicing his bloodthirsty demands in the columns of *L'Ami du peuple*; his medical and scientific interests faded away, though he found time to print and publish in his press: *Les Charlatans modernes* (1791) in which he expressed, in no measured terms, his rage against various members of the French Academy who had refused to accept his views.

As a Deputy of *La Montagne* and a violent journalist, Marat became influential in revolutionary circles; with the help of Simonne Évrard he was able to issue his paper even when he had to go into hiding.

On July 13, 1793, a comely young woman from Caen, Charlotte Corday d'Armand, obtained an interview whilst he was immersed in his bath; after an exchange of a few words, whilst he was writing down some names, she plunged a knife into his right subclavicular space and killed him. She was arrested and after a brief trial executed the same week.

Cesare Lombroso (1835-1909) examined her skull and found it exhibiting all the characters of the prostitute-criminal type. It is not easy to be serious about many of Professor Lombroso's pronouncements, because he would have detected the same features in a turnip grown in a field belonging to Madame du Barry.

THE DIAGNOSIS OF MARAT'S DERMATOPATHIA

Since 1790—approximately—Marat had suffered from a chronic skin ailment which he said had been contracted whilst hiding underground in cellars and sewers; it was located in the groin and scrotum and was characterized by an intolerable itching, which in an irritable individual like Marat, would give rise to rabid scratching with dirty nails—so that the ailment would become worse and worse; the only relief he could find was by prolonged bathing. Cabanés (1911) concluded that it was eczema: Clifford Bax (1901) p. 131 called it *pruritus*, which can be surmised to mean *Pruritus senilis*; this occurs as the outcome of drying of the skin in old age, but since Marat was assassinated at the age of 50, the diagnosis does not seem applicable. Sir Graham Little suggested that it might have been *Dermatitis herpetiformis*, a chronic and troublesome skin disease which resists most forms of treatment. Eczema would be aggravated by prolonged immersion and the instances of *D. herpetiformis* I have seen were not localized like Marat's affection.

One of the latest authors to discuss Marat's skin disease is G.-S. Juskiéwenski—*Jean Paul Marat. Le Médecin, le Savant, le Philosophe, le Journaliste, le Révolutionnaire* (Bordeaux, 1933). This is a graduation thesis and presents the merits and defects of such lucubrations. Juskiéwenski suggests that Marat suffered from diabetes; it may be, but we have no means of deciding. The skin ailment is discussed and the learned opinion of a Professor of Dermatology is quoted; he concludes in a manner that recalls the judgment of Dr. Rondibilis. It seems to me that chronic scabies will fit origin, symptoms and localization; the intolerable itching of scabies would be alleviated by bathing. It might be objected that scabies or "*La gâle*" was well known at the time and treatment by sulphur or mercurial ointment accepted as effective. Still, Marat might well have failed in diagnosing the infestation and would not have consulted others; for at the end of the eighteenth century *Acarus scabiei* was not recognized as the cause of itch, though its parasitic nature had been described by Giovan Cosimo Bonomi (1663-96) and Diacinto Cestoni (1637-1718) in a letter to Francesco Redi; this was published in 1687, but remained unnoticed in medical circles, till 1837 when the Corsican physician, Simone Francesco Renucci demonstrated the mite in the Hôpital St. Louis, Paris. Even to-day the diagnosis is not always easy, as the result of scratch effects and for the same reason, at times, treatment is not effective. During the last war and this, I have seen in women and children instances of scabies which were not recognized under ordinary circumstances.

No doubt the skin disease influenced Marat's temperament and would account for some of his violence.

MARAT'S NECROPSY BY J.-F. LOUIS DESCHAMPS (1824)

It can be mentioned that in a letter to an unknown correspondent (ref. Vellay, 1908, p. 8) Marat refused a request to perform a necropsy; he suggested instead the name of M. Boyer, a surgeon who lived two doors away, Rue de Bourgogne. The letter began: *Ma sensibilité, mon cher Comte, ne me permettant d'assister à l'ouverture du corps d'un ami . . .*

Marat's body was examined anatomically the day after death by the surgeon-in-chief of the *Hôpital de l'Unité, ci-devant Charité*. Cabanés (1911) quoted the full protocol, from which can be gathered that Charlotte Corday's knife had penetrated the space between the first and second right ribs, transixed the lung, gone through the aorta and entered the left auricle. It is noteworthy that the whole surface of the right lung was found adherent to the pleura; so that at some time, Marat must have suffered from pleurisy. This was probably about 1788-89 when Marat made his will, because he was seriously ill.

When Corday killed Marat he was an ailing man; even so, had he survived, it is more than probable that he would have gone to the guillotine, like Robespierre, St. Just, Couthon, Hébert.

Marat was small, about five feet in height, ugly, not an impressive orator; his French pronunciation was not considered perfect; this is strange, because Neuchâtel is one of the places where good French is spoken. Many pictures of Marat are known, but only three or four can rank as accurate portraits.

WAS MARAT REALLY A PARANOIAC?

Those who believe that Marat was a madman are considering the last three or four years of his life, when many of his utterances were those of a homicidal maniac; it is also mentioned, more than once, that he suggested that if he were placed at the head

of affairs, all would be well; that he wished to become legislative and military dictator. A psychiatric diagnosis should be exact in the description of clinical, pathognomonic symptoms and take into consideration antecedents and previous behaviour of the patient. Here it can be said that the lives of father and mother, brothers and sisters of Marat have been followed and no insanity was obvious in any of them. One brother, Henri Mára, went to Russia and became a teacher in the Imperial Military Academy, under the name of Chevalier de Boudry.

Charles W. Burr—Professor of Mental Diseases, University of Pennsylvania—in: *J. P. Marat, Physician, Revolutionist, Paranoiac*, *Ann. Med. History*, 1919, 2, 248-61, justified his diagnosis thus:

"He belongs then among the insane, and is an example of paranoia of the political type. He presents the cardinal symptoms of paranoia, intense egoism, delusions of persecution, and an angry grandiosity. He has a common secondary symptom, viz., unlimited verbosity, the matter of his speeches being always the same, the wickedness of his persecutors, his own virtue, wisdom, and unselfishness. He had the paranoiac's intensity of manner in speaking, and the tremendous verbal diarrhoea which deceives the common man, who, overwhelmed by the cataract of talk, goes home feeling that the orator must be a profound thinker because he talks so well. His moral code was wrong, and yet like all paranoiacs he regarded himself as virtuous."

This discernment is thoroughly supported, but to my way of thinking, "mad" to a medical mind must mean "certifiably insane". It is true that Marat fulfilled one of the conditions for certification; he was a danger to his surroundings, for he could inflame the base passions of the populace so that they resorted to bloodshed and plunder. But it should not be forgotten that until he became cognizant of his power of swaying the mob, he behaved sanely, even if somewhat morbidly.

His egotism was not greater than that noticeable in the autobiographies of Benvenuto Cellini or Giacomo Casanova—to mention the first two names I can recall. His "delusions of persecution"—as Burr calls them—though exaggerated, were not figments of a diseased imagination; when Marat accused Frederick, Lord North (1733-92) of having attempted to suppress "*The Chains of Slavery*" it suited the Deputy of *La Montagne* to paint a dark picture of the machinations of a mouthpiece of King George III. Marat often offended those with whom he discussed scientific matters and they retorted by calling him a charlatan. In the Revolution, his enemies would have gladly taken his life, indeed they got it. His angry grandiosity—his violent verbosity—were they really exceptional or abnormal at the time? The life and behaviour of Robespierre, St. Just, Couthon, Hébert did not differ appreciably from that of *L'Ami du Peuple*. Like them, Marat developed into a sanguinary maniac when he found that by yelling: *Les aristos à la lanterne!* brought him the applause of crowds.

CONCLUDING REMARKS

Carlyle in his *French Revolution*, Vol. II, wrote: "*Prince d'Artois has withal the strangest horse-leech, a moonstruck, much enduring individual.*" It has been seen that Marat obtained a medical degree, practised mainly human medicine and as to being moonstruck or a lunatic—that is a matter of opinion. Marat was not a whole-hearted medical practitioner; he found it a convenient manner for earning a living and to pay for the printing of his philosophical works; but when his practice failed in being remunerative he preferred to revert to his researches on light, fire and electricity. It is evident that he was moderately—quite moderately—successful as a medical practitioner during two or three years in London and Edinburgh—approximately during 1774-75; the vague address "Church Street, Soho" has no real meaning. Had his practice been lucrative then he would not have settled in Paris—for his appointment with the Comte d'Artois was due to Mme de Laubespine's influence. He was very successful in Paris, 1777 to 1780-81, when it was ascertained that he lived in well-furnished apartments in the Rue Bourgogne, Faubourg St. Germain. Eventually his practice declined, as the result of professional jealousy and opposition; he soon had to live penuriously and may well have resorted to different means to make ends meet. Marat's prescriptions can be compared with those of other physicians of his time; they show him to have been a "simplicist", that is, he relied on relatively simple substances for the purpose of treatment. His success with Mme de Laubespine is explainable by the fact that instead of employing antimony, bleeding, &c. his expectant treatment gave the *vis medicatrix naturæ* a chance to improve the health of the patient.

Thus an examination of Marat's medical career allows the conclusion that neither in his methods, outlook or recorded documents, could he be considered a "quack". These abounded in London and Paris at the time; Chevalier Taylor with his florid orations, James Graham and the "Celestial Bed", Mesmer playing on his harmonika, the two Whitworth Farriers, with their "drops" and "red bottles" of medicine, "Dr." Myersbach, the urine-caster and many others besides: all these behaved quite differently from Dr. Marat, whose medical practice seems to have followed orthodox paths.

Section of Experimental Medicine and Therapeutics

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WALTER ERNEST DIXON MEMORIAL LECTURE

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International Biological Standards: Prospect and Retrospect

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SUMMARY

WALTER ERNEST DIXON was one of the first to advocate the biological standardization of drugs; he was interested in the work of the Health Organization of the League of Nations, served on its committees and gave to it freely of his time and advice. The lecture records some of the advances made, chiefly since Dixon's death in 1931, in some of the fields in which he himself had been interested and active.

The need for biological standards and units, early examples of their use, the fundamental concepts and principles introduced by Ehrlich, the effect of the First World War, the pioneer work of Madsen and Dale leading to the birth of the international idea, are described. Subsequent developments and application to a wide range of biological products, and the means adopted for bringing standards and units into use on the widest international scale are described, and the effect on research, clinical medicine, large scale manufacture and public health administration are outlined. The establishment of an international standard and unit for penicillin is dealt with in some detail, the measures taken for replenishing the stocks and preparing replacement standards are described, and the directions and applications in which future developments may be expected to occur are indicated.

To-day we honour the memory of Walter Ernest Dixon, who died fourteen years ago at the age of 60. His friends will recall his charm, his kindly friendliness, and his humour; and to them and to a wider circle he is remembered as a man of wide scientific outlook, interested throughout his life in many of the topics and biological materials we shall discuss to-day, in endocrinology and very specially in the drugs of addiction: and his services to pharmacology, which have had such an important influence on the progress of the science in England, are remembered with gratitude and appreciation. He was one of the earliest advocates of the biological standardization of drugs and his advice was frequently sought by the Health Organization of the League of Nations and he served on several of its committees. It is fitting, therefore, that we should review the progress made, in the period between the two world wars, in some of those fields of scientific activity in which Dixon himself was interested and in which he played a part.

There are a number of substances in common use in medicine the activity of which cannot be estimated by the usual chemical or physical means and for which, accordingly, other methods have had to be devised for the determination of their potency. Many of the more important of these are shown in the table. They are mainly of biological origin and, when first introduced to the laboratory worker or the doctor, they were crude products, mixed up with other substances of equal or greater complexity, devoid of characteristic chemical or physical properties by which they might be identified or characterized and, perhaps, assayed. The usual basis of dosage, by weight or volume, is clearly inapplicable to substances such as these and yet, in the case of many of them, it is obviously very important that the quantity being administered should be known and capable of being adjusted to the needs of the individual patient. The solution to this problem which science has devised is to define their potency in units of biological activity and it is one of the practical aims of biological standardization to provide, for the use of the doctor and the research worker, preparations of which the potency has been accurately determined and expressed in a common system of unit notation and completely accepted.

INTERNATIONAL BIOLOGICAL STANDARDS.

Standard preparation	First adopted	International unit mg.	International distributing centre
Diphtheria antitoxin	1922	0.0028	State Serum Institute, Copenhagen
Tetanus antitoxin	1928	0.1547	
Antidysentery serum (Shiga)	1928	0.0500	
Staphylococcus antitoxin	1934	0.5000	
Antipneumococcus serum (Type 1)	1934	0.0886	
Antipneumococcus serum (Type 2)	1934	0.0894	
Gas gangrene antitoxin (perfringens)	1931	0.2660	
Gas gangrene antitoxin (Vibrio Septique)	1934	0.2377	
Gas gangrene antitoxin (oedematis)	1934	0.2681	
Gas gangrene antitoxin (histolyticus)	1935	0.3575	
Gas gangrene antitoxin (sordelli)	1939	0.1334	
Old tuberculin	1931	—	
Diphtheria antitoxin for the flocculation test	1935	—	
Vitamin A (mixed carotenes)	1931	0.001	National Institute for Medical Research, Hampstead, London
(pure β -carotene)	1934	0.0006	
Vitamin B ₁ (adsorption product)	1931	10.0	
(pure synthetic vitamin B ₁)	1938	0.003	
Vitamin C (<i>L</i> -ascorbic acid)	1934	0.05	
Vitamin D (irradiated ergosterol soln.)	1931	1.0	
(calciferol)	1934	0.000025	
Vitamin E (α -tocopheryl acetate)	1941	1.0	
Arsphenamine	1925	—	
Neoarsphenamine	1925	—	
Sulpharsphenamine	1925	—	
Insulin (crude dry hydrochloride)	1925	0.125	
(pure crystalline)	1935	0.0455	
Pituitary (posterior lobe) powder	1925	0.5	
Digitalis	1925	80.0	
Ouabain	1928	—	
Oestrus-producing hormones :			
(1) Oestrone	1932	0.0001	
(2) Oestradiol monobenzoate	1935	0.0001	
Androsterone (for male hormone)	1935	0.1	
Corpus luteum hormone (progesterone)	1935	1.0	
Chorionic gonadotrophin	1938	0.1	
Serum gonadotrophin	1938	0.25	
Thyrotrophin	1938	—	
Prolactin (galactin or mammatrophin)	1938	0.1	
Heparin	1942	0.0077	
Penicillin	1944	0.0006	

Even in their crudest form these substances exhibit specific biological properties, often unique and quite characteristic, which can be demonstrated by means of animals; and it is these characteristic biological reactions which man has exploited and applied and made to serve as a basis for the determination of their potency. Thus, given two samples of one of these substances, then their relative potency can be estimated by determining how much of each is required to produce the same biological effect: or, if one of these two is taken as the "standard" it is possible to find out how much of any other sample produces the same biological effect as 1 milligramme, or 1 microgramme, or 1 unit of this standard. If the total amount of the standard is sufficiently large, quantities of it can be sent to any laboratory in the world and the potency of substances can be determined in relation to this common standard and expressed in a common system of unit notation. The one essential condition for the successful performance of these potency determinations is that the biological tests upon which they are based shall be carried out under strictly comparable conditions.

The therapeutic substances for which international biological standards have been established and adopted form a very varied group, and their origin and purpose are likewise very diverse. Most of them are of relatively recent discovery, all of them are substances of great biological interest and importance. In so far as they are used in medicine the point immediately emerges that they are not mere palliatives, used for the alleviation of symptoms, but they are specific remedies for the prevention or treatment of disease, or for the replacing of defects or deficiencies from which the human body may be suffering. Some of these substances are potentially dangerous and for their safe and effective use they must be administered by precise dosage. The need for precise measurement is no less great for the research worker in the fields in which these materials are studied or used. Without a common standard, a common basis of measurement and a common

system of notation the results of investigations in different laboratories and hospitals in different countries cannot be correlated and compared.

Expressed in its simplest form, a biological standard may be defined as an arbitrarily chosen but representative sample of the substance for which it is to serve as a basis of measurement, preserved under conditions ensuring its permanence; and, in general terms, a unit may be defined as the specific biological activity contained in a certain weight of such a standard.

The individual laboratory worker, if he chooses, can establish a standard and unit for himself in order that the measurements he may be making at different times can be correlated and compared. The currency of such a standard and unit may extend no further than his own laboratory, unless, of course, a few workers studying the same problems and using the same or similar materials may wish to have a common basis of measurement and then this currency is extended accordingly.

Similarly it might be desirable that all batches, or types or makes of a commodity or drug supplied in a particular country, should conform to certain requirements and it is then proper to establish a standard, and if need be a unit, which would have a national currency and serve the needs and convenience of workers within a national boundary, thus ensuring that statutory requirements are everywhere complied with in that country.

International standards and units are intended to have the highest authority, to be operative on a world scale and enjoy the widest possible currency: and obviously there must be some representative body, properly constituted and having authority, whose decisions and edicts carry weight and are respected if these objects are to be achieved.

Such a body is the Permanent Commission on Biological Standardization of the Health Organization of the League of Nations which was established in 1924. The Commission has had two main objects: (1) To create, establish and provide standards by means of which the potency of certain biological products can be determined and expressed in a uniform system of unit notation; and (2) to secure the acceptance of these standards and units for international use on the widest possible basis.

EARLY ATTEMPTS AT BIOLOGICAL STANDARDIZATION

Looking back from the vantage ground of the solid achievement represented by these thirty-five material standards it is interesting to examine the origins and trace the development of the ideas and the work which led to their creation, to the world-wide interest they have since aroused, and to their extensive application to serve the needs of modern medicine and research. The history of biological standards began half a century ago when physicians using the new diphtheria antitoxin, the discovery of which had been announced by Behring in 1890, found that their clinical studies were seriously handicapped because they were so uncertain about the potency of the antitoxins they were using. Roux and his colleagues, whose communication to the International Congress of Hygiene at Budapest in 1894 reporting the clinical efficacy of diphtheria antitoxin created such a deep impression, attempted with little success to determine potency by a complicated method in which the weight of the animal, the dose of antitoxin given and the time of survival following the injection of living culture all had to be taken into account; and while the early attempts of Behring and the German workers, based on determining the amount of antitoxin which neutralized a certain number of so-called "minimum lethal doses" of toxin was simpler, these like the French attempts, failed because the highly complex nature of diphtheria toxin was not then understood. An appeal was made to Ehrlich, not specially interested at that time in problems of this kind and not yet the world-famous figure which he subsequently became, who was thus led to a series of investigations which not only solved these immediate problems of antitoxin standardization but laid the foundations of what has properly come to be recognized as the modern science of biological standardization. Ehrlich revealed the complexity of diphtheria toxin and explored its various reactions with antitoxin; and his discovery that "toxins" contained in variable amount a substance which, though without toxic action, nevertheless neutralized antitoxin provided an explanation for Behring's bewilderment and failures. As a result of these investigations Ehrlich showed that the only way out of the maze and the difficulties was to adopt a sample of diphtheria antitoxin as a "standard" in comparison with which the potency of other samples of diphtheria antitoxin could be determined; and he also showed that the unit of diphtheria antitoxin was properly defined in terms of this standard, viz. as the specific biological activity (in this case the neutralizing or combining power for diphtheria toxin) contained in a given quantity of the standard—two important fundamental principles; and he passed to a third. He recognized that, since the unit must be a fixed unvarying quantity, it was essential that the standard must also be fixed and stable. Accordingly, since liquid preparations of antitoxin lose their potency slowly with age, Ehrlich reduced the sample of diphtheria antitoxin selected for the standard to the absolutely dry condition and preserved it constantly at low temperatures *in vacuo*.

THE FIRST STANDARDS FOR DIPHTHERIA AND TETANUS ANTITOXINS

This first important standard, for diphtheria antitoxin, was supplied from Ehrlich's Institute at Frankfurt to laboratories all over the world and, although French workers dissented on some points, the great majority of other workers supported Ehrlich's views and confirmed his results; and order and uniformity were introduced into the standardization of diphtheria antitoxin.

In 1905, another and separate standard for diphtheria antitoxin was established at the Hygienic Laboratory at Washington (as this Institute was then known) and the unit of diphtheria antitoxin which Ehrlich had established was defined as a weight of this standard also—an important and fortunate circumstance in the light of subsequent events. Moreover, this work at Frankfurt and Washington had proved so successful in regard to the assay of diphtheria antitoxin that, in both these countries, dry stable standards were established for tetanus antitoxin. At Frankfurt the assay of tetanus antitoxin, in relation to the standard, was on somewhat different lines from those adopted at Washington. The Hygienic Laboratory, indeed, followed the original methods which Ehrlich had applied with such success to diphtheria antitoxin very closely, and the result was that the American standard and unit for tetanus antitoxin were well established and in common use, particularly in the laboratories of the United States and of this country, for some years before the outbreak of war in 1914—another fortunate circumstance.

THE BEGINNINGS OF INTERNATIONAL CO-OPERATION

With the outbreak of war in 1914, the supply of the diphtheria antitoxin standard from Frankfurt ceased at once; and the sudden removal of this essential reagent was one of the facts which led, first, to the establishment of the standard for diphtheria antitoxin on an international basis and, secondly, to the creation and adoption of international standards for other substances. In 1921, thanks to the initiative of Dr. Thorwald Madsen, Director of the State Serum Institute at Copenhagen, an international conference was held in London, under the auspices of the Health Organization of the League of Nations. The immediate purpose of this conference was to ascertain whether the unit for diphtheria antitoxin, based on the standard established at Washington, which had been used in different parts of the world during the war, differed from the original unit established by Ehrlich and maintained at Frankfurt. It was found that no change in the unit value had occurred and the conference recommended the adoption of this original unit of Ehrlich as the international unit. This was an event of great importance to science and medicine; but of even greater significance was the fact that, so shortly after their countries had been at war, men of science could meet together for the pursuit of the common aim of extending our knowledge and promoting the benefit of all mankind. Madsen was a great figure in international science; his country had not been at war and it is to his everlasting credit that he saw this opportunity and seized it so promptly, with such happy and fruitful results.

In the following year a second international conference met in Paris to explore the possibility of establishing standards and units for other antitoxins and antisera. The success of these two conferences led to what we now recognize as a most important milestone—the extension of this international enterprise to substances other than antitoxins but which, like them, could only be standardized by biological methods. During a visit to England in 1922 Madsen, whose major interest was serology and immunology, suggested to Sir Henry Dale that something on similar lines might be done for other substances. The heart drugs, extracts of the posterior lobe of the pituitary body, the arsphenamines (for which during the war Dale himself had devised biological tests for their control) and insulin all presented problems similar to those which had arisen in the case of antitoxins and, as fortunately proved to be the case, capable of solution on similar lines. The outcome of all this was that an international conference was held at Edinburgh in 1923 followed by one in Geneva in 1925, Dale being chairman on both occasions, at which international standards for digitalis, pituitary (posterior lobe) extract, insulin and the arsphenamines were agreed upon and adopted.

THE PERMANENT COMMISSION ON BIOLOGICAL STANDARDIZATION

The marked success of these early conferences led to the formal institution in 1924 by the Health Organization of the League of Nations of the Permanent Commission on Biological Standardization. This was a small body of experts chosen for their scientific qualifications and attainments, all interested in some aspect of biological standardization, and regardless of whether their countries belonged to the League or not. Dr. Madsen has always been the Chairman of this Commission and, right from the beginning, Sir Henry Dale has been the sole representative of this country on the Commission and, indeed, almost the sole representative for the biological standards for drugs, vitamins and hormones. The other members of the Commission were experts from France, Belgium, Germany and the United States. The personnel was enlarged somewhat in 1935.

The international standards for the antitoxins, antisera and for tuberculin are maintained at the State Serum Institute at Copenhagen, while the international standards for all other substances—insulin, pituitary extract, the arsphenamines, the vitamins, the sex hormones, the heart drugs, heparin and penicillin—are maintained at the National Institute for Medical Research at Hampstead. From these two international distributing centres the standards are supplied to laboratories, institutes and research workers throughout the world; and by thus providing a common basis of measurement and a uniform system of nomenclature and unit notation, the results of research, whether in the laboratory, the hospital or the field and in whatever country, can be correlated and compared. The

use of the same standards and units are of no less importance to the manufacturer who can compare his products with those made in any other laboratory and provide them for use in any other country; their adoption has greatly facilitated the international exchange of these substances whether for the treatment or prevention of disease or for purposes of research. The practical advantages and benefits of a universally acknowledged and accepted system of standards and units are greatest, perhaps, in clinical medicine; by their use the authenticity, potency and quality of these important therapeutic substances are controlled and, very largely, guaranteed; and doctors and patients can obtain, for their use in other lands, drugs and remedies, such as insulin, for example, which are as reliable as those which they have been accustomed to use in their own country.

The Commission has had a twofold purpose—first, to provide international standards and units as and when they are required and, secondly, to secure their adoption and effective application on a wide international basis. It is not always easy to decide whether a standard should be established at a particular time; if action is taken prematurely an unsuitable standard or a unit of unsuitable size may be adopted, while if action is unduly delayed there is the opposite danger that a multitude of different units which may be quite unrelated or impracticable may be proposed, brought into local or national use, defended by a powerful advocacy or a stubborn persistence and withdrawn or modified with reluctance. On the whole the Commission, partly by judicious choice of the appropriate moment to take action and partly by the display of a wide toleration and a wise compromise, has been remarkably successful in securing agreement in essentials. When delegates meet in conference important factors such as the suitability and availability of the material to be used as a standard, whether there are methods of assay available and the order of accuracy of their application, the merits of rival claims for a standard or unit, and other such matters appear in their due perspective and are discussed in their proper relation to the main points at issue; and in the end, by inquiry, investigation, discussion and conference, added to and aided by the co-ordinated research in many countries and many laboratories which has been carried out, chiefly by the delegates themselves prior to the Conference, agreement is reached. Only once has there been serious disagreement, and as this occurred early in the development of this work and the consequences have been so disastrous, it may be that this single failure to achieve agreement (concerning the unit of tetanus antitoxin) served as a warning for the future.

INTERNATIONAL UNITS

A unit is properly defined as the specific biological activity contained in a given weight of the standard preparation; and, in the table, in regard to 28 of these 35 substances, the weight of the respective international standard which has been accepted as the international unit is recorded. It will be noticed that these weights vary from a fraction of a microgramme to as much as a milligramme, and, in the case of digitalis, to the large value of 80 milligrammes.

The size of the international unit has been arrived at in different ways. Sometimes a unit which has become established through common usage, as in the case of diphtheria antitoxin and penicillin, has been recommended for adoption by the Commission; and sometimes an arbitrarily chosen weight of the standard is adopted as in the case of antidyentery serum and staphylococcus antitoxin. Frequently, however, the size of the unit recommended for adoption is either the result of compromise between conflicting claims, or (and perhaps more commonly) it results indirectly from the Commission's successful substitution of sound principle for fallacious reasoning and argument. Thanks to a generation of sound teaching and effective advocacy, it is now becoming more generally recognized that potency cannot be determined, and units of activity cannot be defined, by simple observation of the effects produced on an animal, or, as it is expressed, in terms of an animal reaction; that this is because of the wide variation in animal response to the same biological stimulus; that this factor of animal variation, more than any other, dominates the whole field of biological standardization, and that it can only be controlled and allowed for by the adoption of standard preparations and by carrying out the biological tests on the standard and the sample of unknown potency under strictly comparable conditions. In the past, it was only too common to find that, when a substance with biological activity and possibly clinical application was discovered, a unit of activity was proposed which was defined as the quantity which produced a certain biological effect. Thus, it was proposed that the unit of insulin should be defined as the quantity which reduced the blood sugar of a rabbit to a certain low level, the unit of a vitamin as the quantity which restored growth, and so on. A very few experiments showed that these quantities were very far from being constant; they varied in different laboratories, from one animal to another and from day to day in the same laboratory. Now, very often the size of an international unit bears some rough and approximate relationship to the biological effect it produces; for example, the unit of insulin is a quantity which reduces the blood sugar of many fasting 2 kilogram rabbits to the convulsion level, but it does not produce this effect with all rabbits, and not always with the same rabbit, and not with

regularity. In conferences called by the Commission to decide about standards and units, it has frequently been possible to get those who rightly believed that the unit should be a weight and those who wrongly believed that it should be an animal reaction to reach agreement by fixing the unit at, or about, the weight which usually produced the particular biological reaction which, to some of the delegates, appeared to be the kernel of the matter. But from all these discussions and conferences the final definition of the unit recommended for adoption is always the same, viz. the activity contained in a certain weight of the standard and, as the standard is a dry stable substance, so also is the unit fixed, definite and unchanging.

One consequence of this desire to reach agreement in regard to units of activity has been that the size of the unit adopted for international use has not always been the most practicable and best suited to the needs of medicine; occasionally the unit adopted has been so small that the dose of the drug administered to patients has reached astronomical figures. Many factors, known and appreciated better perhaps by a body like the Commission than by an individual laboratory worker or physician, enter into the question as to what constitutes a suitable unit; and it would be an advantage, in the future, if questions relating to the unit could be left to a body with experience like the Permanent Standards Commission.

PREPARATION AND PROPERTIES OF BIOLOGICAL STANDARDS

One essential of a biological standard is that it shall be stable, and this requirement is met by preparing it in the absolutely dry condition and preserving it constantly at low temperatures, in sealed containers, in the absence of light, moisture and oxygen. Although the materials for these standards have come from many countries, the final operations to secure these conditions of permanency and stability for twenty-eight of them have been carried out in England and, for twenty-four of these, at Hampstead during the past twenty years. Ways and means have had to be devised, varying with the particular standard but appropriate to each, for providing these conditions for ensuring stability. When this work was begun at Hampstead over twenty years ago there was little more than the experience and teaching of Ehrlich to go upon, but it seemed reasonable to expect that if the possibilities and opportunities for chemical and physical change were reduced to the lowest attainable minimum, then the standards should undergo no change. It may now be claimed with some confidence that these expectations have been realized.

Except in the case of tuberculin the basic standard is a dry preparation, and each standard is dispensed so that it is readily accessible and capable of being brought into use with a minimum of trouble, extra manipulation and delay. Since world needs are to be met, and for long periods, the quantity set aside for use as an international standard must obviously be very large, and the stocks held at Hampstead at present are adequate for world needs for very many years.

Five of the original international serum standards were made at Hampstead and a number of equivalent national standards have had to be made for the purpose of the British Therapeutic Substances Act and the British Pharmacopœia; and during the war replacement standards, on the international account, for perfringens, septicum and œdematients antitoxins had to be prepared.

A method for preparing serum standards was devised in 1923 (Hartley, 1935) and has been widely used in many laboratories since that time.

By this method a very large number (several hundreds) of sealed ampoules, each containing the same weight of standard antitoxin in the dry stable condition, is obtained and it is only necessary to determine, once and for all, the number of units present in an ampoule, and the preparation of the usual standard solution is then made as required and distributed to laboratories all over the world.

This is a very simple method: the different stages are easily controlled, sterility is maintained without any difficulty, and only ordinary laboratory apparatus is required. The final product is very stable. The defects of the method are that it takes several weeks to complete the operations and, although there is no loss of potency during drying, the final product dissolves rather slowly. These are defects which will be overcome in the future by drying from the frozen state by one of the methods which have been devised and used during the war. Further, it is quite practicable to prepare standards for substances other than antitoxins by making solutions of them, distributing precise volumes into ampoules, and drying them from the frozen state.

The International Sources of the Materials for the Standards

To illustrate the international character of this work it may be stated that the material for the serological standards has been supplied from Denmark, England, France and the United States; the tuberculin standard was made in England; material for the vitamin standards came from Switzerland, the Netherlands East Indies, Hungary, England, France, Germany, Sweden and the United States; that for the arspenamines was provided originally from Germany and the United States and, since 1935, from England; the first insulin standard was made in England, the second in Canada; the material for both of the pituitary (posterior lobe) standards was supplied from the United States and manipulated into a standard in England; the first digitalis standard was prepared in Holland, the second in England; the ouabain standard was supplied from France. The materials for the sex hormone standards, some of them rare and costly, were supplied from England, France, Germany, Holland, Denmark, Sweden, Switzerland and the United States. Canada provided the material for the heparin standard, and the United States and this country that for the penicillin standard. It is very gratifying to record, and may be taken as evidence of the esteem in which this work is held, that practically all the material for these standards has been presented to the international organization, and some of these gifts represent very large sums of money. A laboratory in Switzerland presented 30 grammes of androsterone to provide the material for the replacement of the standard for male hormone activity; one laboratory in England presented 20 grammes of the purest Beta-carotene to provide the material for the replacement of the standard for vitamin A, and another has presented 30 grammes of the sodium salt of pure crystalline penicillin II for the use of the Department of Biological Standards at Hampstead. The League, on its part, makes no charge whatever, neither to countries nor to individuals, for the supply of the international standards. And it may be added that free distribution is the invariable rule for all standards issued from Hampstead on a National basis, or to, the British Commonwealth of Nations or to individual research workers. Whatever changes the future may hold, it is to be hoped that this free distribution of biological standards will be everywhere maintained.

The Establishment of Standards and Their International Distribution

Brief reference will be made to the course of events which led to the adoption of international standards for the vitamins and to the subsequent developments in this field as this will serve as a particular instance to illustrate the procedures followed by the Permanent Standards Commission which have been outlined in general terms, first for the establishment of standards and, secondly, for securing their widespread acceptance and application.

The main decisions were reached at two international conferences held in London, the first in 1931 and the second in 1934, Sir Edward Mellanby being Chairman on both occasions.

Prior to the first conference a number of laboratories in several countries were becoming concerned about the assays of the vitamins B₁ and D. As on other occasions there was much and increasing confusion because of the multiplicity of units—pigeon units, rat units, guinea-pig units and so on—which had been proposed, all based on animal reaction, all unsound in principle and all impossible of wide-scale application in practice. Actually one of the first tasks at that first conference, as on so many other occasions, was to convince all the delegates that the only way to solve these problems was to adopt stable standards and define units in terms of them. Having before it the results of the examination of a sample of carotene prepared in England, a preparation of Vitamin B prepared in Java, and a sample of irradiated ergosterol prepared in England the first conference had no difficulty in recommending the adoption of these as provisional standards for a term of years for the vitamins A, B₁ and D and of defining units in terms of them.

Certain other investigations were planned and other materials were examined later, so that at the second international conference held in 1934 pure Beta-carotene was adopted as the standard for vitamin A, the adsorbate on fuller's earth was continued for that for vitamin B₁, ascorbic acid that for vitamin C and calciferol as the basic standard for vitamin D. A third international conference, also to be held in London, was planned for 1939, but had to be abandoned and some of the more important and urgent matters have had to be settled in other ways.

Although it is not included in the table, it should be mentioned that all the first international conference was able to recommend for use as a standard, in 1931, for vitamin C, was the juice of a lemon, the unit recommended being 0.1 c.c. But even this was better than nothing and better than a unit defined in terms of an animal reaction because, in less than three years, ascorbic acid had been discovered, its identity with vitamin C established and its synthesis achieved. There was no difficulty about adopting ascorbic acid as a stable standard for vitamin C and the international unit was actually determined in relation to this first crude vitamin C preparation.

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One consequence of this desire to reach agreement in regard to units of activity has been that the size of the unit adopted for international use has not always been the most practicable and best suited to the needs of medicine; occasionally the unit adopted has been so small that the dose of the drug administered to patients has reached astronomical figures. Many factors, known and appreciated better perhaps by a body like the Commission than by an individual laboratory worker or physician, enter into the question as to what constitutes a suitable unit; and it would be an advantage, in the future, if questions relating to the unit could be left to a body with experience like the Permanent Standards Commission.

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Five of the original international serum standards were made at Hampstead and a number of equivalent national standards have had to be made for the purpose of the British Therapeutic Substances Act and the British Pharmacopœia; and during the war replacement standards, on the international account, for perfringens, septicum and œdematians antitoxins had to be prepared.

A method for preparing serum standards was devised in 1923 (Hartley, 1935) and has been widely used in many laboratories since that time.

By this method a very large number (several hundreds) of sealed ampoules, each containing the same weight of standard antitoxin in the dry stable condition, is obtained and it is only necessary to determine, once and for all, the number of units present in an ampoule, and the preparation of the usual standard solution is then made as required and distributed to laboratories all over the world.

This is a very simple method: the different stages are easily controlled, sterility is maintained without any difficulty, and only ordinary laboratory apparatus is required. The final product is very stable. The defects of the method are that it takes several weeks to complete the operations and, although there is no loss of potency during drying, the final product dissolves rather slowly. These are defects which will be overcome in the future by drying from the frozen state by one of the methods which have been devised and used during the war. Further, it is quite practicable to prepare standards for substances other than antitoxins by making solutions of them, distributing precise volumes into ampoules, and drying them from the frozen state.

The actual international standard preparations obviously cannot be used for the routine assays of penicillin as the total quantity available is far too small; they are supplied for the assay and periodical check of equivalent national standards which the national control centre of each country is, quite properly, expected to prepare. The national control centre will then supply its national standard, exactly assayed in terms of the international standard, to all those laboratories requiring it in its own country and, with this, each laboratory will assay, and check periodically, its day-to-day working standard.

The first preparation used for providing a means of assaying the activity of penicillin samples prepared in different laboratories was supplied by Florey and his colleagues from Oxford and the unit of activity, which came to be known as the Oxford Unit, was defined as the activity contained in 0.23 milligramme of this first preparation. It was supplied to workers in this country and in the United States and, one way and another, this original Oxford Unit was re-defined in many other more active preparations. For the purpose of establishing a standard for use in connexion with the British Therapeutic Substances Act, the Hampstead Institute was provided with two such accurately assayed preparations, one of which contained 71 and the other 84 units per milligramme. With these the potency of the British standard for penicillin was determined with the greatest possible precision. These three English penicillins and two accurately assayed preparations from the United States, which conveyed the American version of the original Oxford unit, were included in the samples examined for the London Conference. Three most interesting conclusions emerged from the results of the comparative tests carried out, in this country and in North America, on these samples. First, the results of the assays showed remarkably good agreement despite the different methods employed by the collaborators. Second, there was good evidence that the value of the unit being used was the same in the United States as in this country, from which it certainly seems that, despite the repeated re-definition of the unit in both countries, the original value of the unit as defined at Oxford had not been significantly varied in its value in either country—a very remarkable result. Third, the conference pointed out that the value of the unit recommended for international use was approximately equivalent to that originally adopted at Oxford. The wheel had thus come full circle; just as the unit established by Ehrlich for diphtheria antitoxin was afterwards adopted as the international unit so here, too, international status has been accorded to a unit which had its origin in the laboratory where so much had been done, in those early difficult times, to bring the fruits of Fleming's great discovery within the reach of all.

International Biological Standards in the Service of Medicine

Another circumstance which has contributed towards a wide distribution of the international biological standards is the recognition of the important part they play in ensuring the high quality of the therapeutic substances provided for use in medicine, for which they serve as standards. This may be illustrated by reference to British practice and experience.

For nearly twenty years the supply of certain drugs and medicaments in this country has been controlled by means of the Therapeutic Substances Act. In general terms these materials are described as "Substances the purity and potency of which cannot be adequately tested by chemical means"; and many of the most important of them—the anti-toxins and tuberculin; insulin, pituitary extract and the arsphenamines—are listed in the table, and for all of them international standards have been established. Stated quite simply, the Therapeutic Substances Act requires that the potency of the substances controlled by it shall be expressed in terms of the international standards and units, and in no other. But this Act, excellent and effective as it has proved to be, is limited in scope and in its geographical application. Its control does not extend to the vitamins nor the heart drugs for example, and the sphere of its application does not extend beyond Great Britain and Northern Ireland. A way has been found, however, whereby both of these limitations may be overcome and many of the undoubted benefits and advantages of the Act made to operate in a wider field. This has been done by bringing the substances for which international biological standards have been established within the scope of the British Pharmacopœia; and the Pharmacopœia, on its part, has laid down the principle that the standards and units to which pharmacopœial preparations must conform are the international biological standards and units.

In many parts of the British Commonwealth and Empire, in Canada, South Africa and in India, for example, a control over these substances similar to our own has been established, and in these countries also the international standards are in general use. In other parts of the Commonwealth and Empire matters have not yet advanced so far; but, in many of these countries, the British Pharmacopœia has statutory authority, and

Experience at Hampstead has shown that it is one thing to make a standard, assay it, dispense it and get it accepted by the League; it is quite another problem to get it brought into use on a wide international scale. Quite early in this work it was noticed that the standards which had been adopted and were available were not being asked for and were not reaching the laboratories of the world. They looked like becoming museum specimens. In order to ensure that the vitamin standards reached the laboratories where they were required and, it may be added, in order to simplify the administrative problems at Hampstead, countries were invited to nominate national distributing centres and to indicate how many laboratories in each country required each of the vitamin standards. Twenty-three countries did so, and these received the very large supplies they required at once, and these were easily replenished as required. Nine countries failed to nominate national distributing centres and it was actually found that hardly any of the standards reached these countries. So, successful had this scheme been with the vitamin standards that, later in 1935, at an intergovernmental conference at Geneva, it was extended to all other standards and all other countries, and by the spring of 1939 thirty-five countries had made a start with the establishment of a national control centre to deal with standards. One important consequence was that in the early months of 1939, before the outbreak of war in September, there was no difficulty in sending large consignments of the international biological standards provided from Hampstead to all those thirty-five countries and in this way the threatened shortage of these essential materials was largely averted. But this care and distribution of the international standards was only a beginning of the work of these national control centres: it was hoped and intended that many countries would establish and maintain such a centre and thus arouse an interest in this field and stimulate research into the varied problems which are continually arising in regard to the standards and the methods of their application.

This aspect of the problem of international standards has been described in some detail because experience of this work at Hampstead has clearly shown that the establishment of national control centres has been the means of securing a wide international recognition, distribution and application of the standards, and it has aroused a real and active interest in places which might otherwise have remained uninformed and passive in standards, units and assay. The policy of international co-operation on the widest possible basis should be adopted and extended in any further schemes which may be established for the continuation of this work.

The International Standard and Unit for Penicillin

The establishment of the first biological standard by Ehrlich has been described and it may be appropriate to say something of the latest standard—what in fact may prove to be the last standard—established by the Permanent Commission on Biological Standardization, viz. the international standard for penicillin. This provides another illustration of the way the Permanent Standards Commission has approached its problems and attained its objects.

For many reasons it was desirable that an international standard and unit for penicillin should be agreed to and established without delay, so that a unit of penicillin would always mean the same thing, not only at the present time when all this work is being pursued by highly skilled experts in a few countries, but in the future when penicillin comes to be made by others, not so expert, in other countries. It is a remarkable fact that, even in wartime when transport and the circumstances of our daily life were as difficult as they well could be and everybody was very busy, it was possible for the Permanent Standards Commission to fulfil its traditional rôle, at any rate in essentials and even if in a somewhat restricted manner, by bringing together experts on penicillin into conference to advise and decide on these important matters. Delegates from the United States and Canada, from France, Great Britain, and Australia, and expert observers from all these countries and from India and South Africa, met at the Royal Society's rooms in October 1944 under the chairmanship of Sir Henry Dale. After the consideration of certain assay data provided by those attending the conference and of other relevant matters concerning nomenclature, standards, units and methods of assay, the conference unanimously recommended the adoption of a sample of pure sodium salt of penicillin II as the international standard; and, for practical reasons which were certainly justified at that time, the adoption of a sample of a calcium salt of penicillin as the international working standard. The international unit was defined as the specific penicillin activity contained in 0.6 microgramme of the international standard and an international unit is contained in 2.7 microgrammes of the international working standard. The conference recorded other decisions relating to nomenclature, how the material for the standard was to be acquired, finally prepared and dispensed; and directed that the standards should be held by the Department of Biological Standards at the National Institute for Medical Research, Hampstead, on behalf of the Permanent Standards Commission of the Health Organization of the League of Nations and supplied therefrom to all requiring them throughout the world.

standard; and then it is necessary to ensure that the new sample is assayed with the greatest possible precision in terms of the original standard so that the value of the unit is maintained at its exact international value. It is the invariable practice to enlist the co-operation of such experts in this and other countries as are available and willing to carry out these fundamentally important comparative assays.

These replacement operations have provided the opportunity for international co-operation both in scientific research and in the application of its results to the practice of medicine. The first insulin standard was prepared at Hampstead by Dudley and the international unit for insulin was then fixed for all time and defined as the specific insulin activity contained in one-eighth of a milligramme of the standard. This first standard lasted for ten years, but towards the end of its currency period it had come to be questioned whether it could still be accepted as a representative sample because manufacturers were then preparing much purer insulins, containing over twenty units per milligramme, and these differences in quality occasionally showed up in the comparative assays for potency. So in this case replacement became necessary on the dual grounds of exhaustion of the stocks of the first standard and its qualitative disparity from the insulins of commerce. The work of Abel and Scott made it possible to replace this first, rather crude, international insulin standard by an adequate quantity of pure crystalline insulin and the unit value of this was determined with great precision in many laboratories in Europe and America, and it was finally agreed that this value was 22 international units per milligramme.

The replacement of the first international standard for pituitary (posterior lobe) extract presented peculiar difficulties but, at the same time, intriguing scientific problems. This standard is unique in the sense that the international unit is an optimal, rather than a fixed arbitrary value, and there was no doubt that when the new and old standard preparations were compared the new was some 12% more potent than the old. It will probably never be known whether this discrepancy was due to the adoption of a superior technique for the preparation of the replacement standard, whereby a more efficient dissection of the gland, better refrigeration and quicker working gave a final product which actually yielded that maximum activity which it was intended, and expected, all such preparations would give; or whether the original standard during the fourteen years of its currency had lost potency to the extent of about 1% per annum. This instance is mentioned because, apart from its technical interest and its importance to the whole work of biological standardization, the difference was revealed as a result of co-ordinated comparative tests carried out in thirteen laboratories in five different countries. The consequences of these findings and the alternative procedures for action which could be taken were discussed and settled by international action and a solution of the difficulty, satisfactory to all countries and all interests concerned, was reached.

The original standard for vitamin B₁ was an adsorption product of the active material on fuller's earth and the international unit was defined as the specific activity contained in 10 milligrammes. For seven years this standard served for the assay of vitamin B₁, but during all this time purer preparations of the vitamin were being made and tested against this first crude standard until, finally, the pure synthetic aneurin hydrochloride emerged and was found to contain 330 units per milligramme. Thus, while the unit for vitamin B₁ remains unchanged it is now possible to define it in terms of a pure crystalline chemical substance. Similarly, while the first standard for Vitamin C was the juice of a lemon this quickly gave place to pure ascorbic acid, and the pure chemical substance calciferol became the international standard for vitamin D in place of irradiated ergosterol.

The international standards for œstrone, androsterone and progesterone were replaced by new samples of the same materials. Since these are pure chemical substances their replacement presents less difficulty because the assurance that the new material is in close agreement, and even identical, with the original standard is forthcoming from a determination of the chemical and physical constants of the two standard preparations. During the war, and in consequence of it, the stocks of the standards for the three important gas gangrene antitoxins, *Cl. perfringens*, *Cl. septicum* and *Cl. œdematiens* had to be replenished to meet the largely increased demand for them in many countries. It is well known that antitoxins may exhibit abnormal properties and, accordingly, particular attention was given to the selection of the samples which were to replace the original international standards. Although the comparative tests on the old and new standard preparations were somewhat limited on account of wartime conditions there is every reason to believe that the replacement standards are representative and have proved satisfactory.

it is within the powers of medical expert advisers in such countries to require that the potency of drugs used within its boundaries shall conform to the requirements of the British Pharmacopœia; and in this way the international biological standards are being brought into use in other lands.

In view of its varied activities and responsibilities, the Medical Research Council has been able to make an effective contribution to this important matter of bringing the international biological standards into effective operation on the widest possible basis. First, on behalf of the Health Organization of the League of Nations it has accepted the responsibility for the final preparation, dispensing, care, storage and supply on a world basis of all the standards except those for antitoxins, antisera and tuberculin: secondly, it has undertaken a similar responsibility, in respect of this group of the international standards, to the Ministry of Health as regards the Therapeutic Substances Act, and thirdly, a like responsibility to the British Pharmacopœia. But the Council's obligations go further than that, because it is also required to supply standards for the antitoxins, antisera and tuberculin, in whatever country these are made and supplied under licence in accordance with the requirements of the Therapeutic Substances Act. Because of these obligations the Department of Biological Standards at Hampstead has had to prepare and maintain standards for antitoxins, antisera and tuberculin; and these are either part of the actual international materials, or they are national standards which have been exactly assayed. The maintenance of these national standards for antitoxins, antisera and tuberculin has not proved difficult, because six of them had been prepared originally at Hampstead and, when handing them over to the international organization, a sufficient quantity of each had been retained to serve the needs of the British Commonwealth and Empire; and very large quantities of equivalent national standards, which have been checked repeatedly at regular intervals with the corresponding international standards maintained at Copenhagen, are also available at Hampstead. The advantage of this additional source of supply of the international antitoxin and antiserum standards was demonstrated in April 1940, when the supplies held at Copenhagen became no longer available to many laboratories which had hitherto drawn their supplies therefrom. In response to a request from the Health Organization of the League of Nations the Medical Research Council was able to supply these standards from the stocks at Hampstead to any applicant requiring them and was glad to make this contribution towards the maintenance of an essential international service.

In a similar way the international standards have become recognized and brought into use in the United States, through the operation of the National Institute of Health and the United States Pharmacopœia, and it is hoped that they will become established in more and more countries through the action taken by national pharmacopœias. Through other activities of the Health Organization at Geneva good progress has been made towards the unification of pharmacopœias and in this way, too, the international biological standards and units may be expected to receive extended recognition and application.

The table shows that the rate of progress of this work has been steady, continuous, and indeed rapid and it did not stop entirely during the war since the standards for vitamin E, for heparin and for penicillin were adopted in this period. At the end of 1938 practically every country in the world was receiving some or other of the international biological standards. The basis for a world-wide organization had then been created and its development was arrested only by the outbreak of war.

The Replacement of International Biological Standards

Since these 35 standards were established it has been necessary to replace more than 20 of them. In some cases this was because the world demand was so unexpectedly large that the first estimates and supplies were on an entirely inadequate scale: in other cases, as for example the standards for androsterone and progesterone, the world stocks of the standard material available at the time of their adoption were so small that the first supplies were absorbed almost at once. In some cases replenishment became necessary because the existing standard no longer conformed to the manufacturers' products of higher purity which advances in knowledge had made possible. Whatever the cause, the work of providing these replacement standards is among the most onerous and exacting which is undertaken at Hampstead on behalf of the Commission because upon its efficient performance and its precision depends the integrity of the international units. With every such replacement it is first necessary to ensure that the material selected for the new standard is representative and satisfies every condition originally or subsequently laid down by the Permanent Standards Commission for that

become the antigen of choice in many countries. During the war this subject has been investigated in some detail at Hampstead and the results suggest that biological standardization of diphtheria prophylactics is practicable, although the form may be different from that which has been attempted elsewhere and hitherto, and international agreement may be forthcoming.

During this war the efficacy of tetanus toxoid for the active immunization of man has been proved beyond doubt, and a uniform system of assessing the potency of these preparations is desirable and here, again, international action might very well become an early priority for the consideration of the new international organization. Investigations carried out at Hampstead during the war suggest that comparative methods of assay, in relation to a standard, using guinea-pigs as test animals may be practicable; in Canada and India mice are favoured as test animals, and an early question for study would be to determine whether the results obtained are independent of the species of animals used. This investigation might also throw some light on the perennial problem of the complexity of tetanus toxin and antitoxin.

Some of the investigations which we have had to carry out at Hampstead regarding the standards for, and the assay of, the gas gangrene antitoxins which became urgent and important because of the immediate needs of the war also indicate new directions in which this work may develop. After the war had been in progress for some time doubts were expressed as to the adequacy of the international standard for gas gangrene antitoxin (perfringens)—commonly known during the war as Welch antitoxin. Briefly, the criticism was that while the standard provided the means for the assay of α -antitoxin, other activities of the organisms, such as its power to produce hæmolysins and hyaluronidase and the bearing of these on infection, and of the antibodies to them in the control of the disease, had not been taken account of and provided for. This was a serious criticism because, if these other antigens were of significance and importance and if the antibodies to them could be shown to be important in the control of the disease then clearly these antibodies should be provided in Welch antiserum in adequate amounts which could be measured by reference to a more complete international standard, or a series of standards which, it was suggested, should be provided. The whole subject was investigated by Dr. D. G. Evans in the only way available at Hampstead, i.e. by the experimental method in laboratory animals. The results of Evans' work are interesting and important: by carefully controlled quantitative experiments he has shown that α -toxin is the most important product of the Welch bacillus which he has investigated up to now, as far as the infection of guinea-pigs is concerned, that its production in culture is closely related to the virulence of the organism, and that the antibody to this toxin is extraordinarily effective in prophylaxis and, provided the conditions for its administration are favourable, it is reasonably effective as a therapeutic agent in animals in which the infection has not proceeded too far. He has not been able to assign a similar importance to other antigens in the infection due to *Cl. welchii*, nor to their antibodies in the prevention or treatment of the infection in guinea-pigs. These results are interesting for two reasons: first, work in this field does not end with the preparation of a standard, but it is often—as in this instance—the starting point for new investigations. The results of these experiments, on a strictly comparable and quantitative basis made possible by the very existence of the standard and unit, have provided new information and new suggestions and ideas concerning the action of antitoxin in controlling a rapidly progressive fatal infection in susceptible animals; and secondly Evans' work has indicated an approach, by *in vivo* methods, to the study of multiple antigens and their corresponding antibodies which, among other things, may enable those concerned to decide which of these antibodies are of importance and, accordingly, for which of them standards should be established.

International biological standards may find useful application in the rapidly developing field of chemotherapy. Pure substances can usually be fully described in chemical and physical terms, the doses to be administered can be expressed as a weight, and biological standards and units are neither necessary nor desirable. It is otherwise, however, in the case of substances of proved biological activity and clinical usefulness of which the chemical composition is unknown and of which, it may be, successive batches exhibit varying biological properties. For such substances, and in the interim period pending the discovery of their chemical composition and structure or of a more reliable process of manufacture, experience has shown the value of the adoption of a standard by comparison with which other preparations can be matched. And similarly, it is not unreasonable to suppose that penicillin is but the beginning and forerunner of similar substances with antibiotic properties and, as the chemical nature of these may

Purified protein derivative (P.P.D.), which is virtually the active principle of tuberculin in solid form, is now so easily prepared and characterized, and is obviously so much more suitable for use as a standard than the crude "old tuberculin" which has hitherto served for this purpose that its adoption as the international standard is a foregone conclusion. Moreover, the replacement of the liquid "old tuberculin" by a stable solid preparation provides the opportunity for defining a unit of tuberculin activity, and this might be useful in human and veterinary medicine in interpreting and comparing the results of tuberculin tests in different animal species.

FUTURE DEVELOPMENTS

In this inter-war period, then, through the activities of the Permanent Commission on Biological Standardization, biological standards have been established for thirty-five important substances, and those who have been intimately concerned with this work hope to see a new international organization created to maintain and extend it.

It is quite likely that one of the first things such a body would do would be to examine and revise the list of standards enumerated in the table. Science and medicine have moved fast and far in recent years and, for various reasons which we can appreciate and with which we might agree, the new Commission might decide that standards for the antisera and some of the antitoxins could be dispensed with and that arsphenamine, the original "606", has surely earned an honourable retirement. The position of the vitamin standards might also come under review because, thanks to the establishment of biological standards and units and the sound principles of assay which these gave, progress towards their isolation in the pure condition, the determination of their chemical nature and in some cases their synthesis have been so rapid that now, not only have the original crude materials used as standards been replaced by pure chemical substances, but chemical and physical methods for their assay—so much more precise, quicker, economical and satisfactory than biological methods—are available for some of them, and likely to be forthcoming for the others. For methods of biological assay are adopted, not as a matter of choice, but more often through dire necessity as the only means of determining the activity of important remedies; and when in addition dosage is no longer on a basis of units but on the more customary basis of weight the question may well be raised as to whether these vitamin standards and units are any longer necessary. As Dale has picturesquely put it "the ultimate aim of all progressive work on biological standardization, as of all preventive medicine, may be regarded as self-extinction". Partly for the same and partly for other reasons the new international body might bring under review the position of the standards and units for some of the sex hormones. Accordingly the number of international biological standards and units maintained at the present time might be very materially reduced.

Developments during the war years indicate some of the directions in which biological standardization may be expected to advance when peacetime conditions and activities are fully restored.

The standardization of the diphtheria prophylactics is a problem of outstanding importance and urgency. Work in this field had been begun under the auspices of the Commission many years before the war but little progress had been made. This may be ascribed, in the main, to the difficulties inherent to the assay of antigens, and this is due to the extreme variability in the animal reaction to antigenic stimulus; in such circumstances very large numbers of animals are required if the comparative tests for potency are to be of quantitative value and significance. Thus, in Germany where a formol-toxoid standard has been established, 250 guinea-pigs are required for the carrying out of the assay in the way required by Frankfurt. Moreover, the fact that different types of prophylactic were used in different countries complicated the situation and made international agreement difficult. In France, Canada and most of the countries on the European Continent the use of formol-toxoid prevailed. In the United States of America, although practice was passing over to the use of alum-precipitated toxoid, at least two other antigens were being used, while in this country alum-precipitated toxoid and toxoid-antitoxin floccules were the antigens of choice, formol-toxoid and toxoid-antitoxin mixture being favoured in certain areas, but on the whole passing out of use. Accordingly, even if simple, practical, economical and reasonably accurate methods of comparative testing had been available, more than one standard would have been required. In these circumstances it is hardly to be wondered at that in many countries—Britain, Canada and the United States for example—the official requirements called for little more than proof of identity and of some evidence of antigenic activity. The post-war situation, however, offers some prospect of progress in this field; the varieties of antigen have been reduced somewhat, the use of alum-precipitated toxoid has increased and bids fair to

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The full control of any disease or morbid state is almost invariably achieved in three distinct stages, the first in which the condition is recognized and defined, the second in which the clinical and laboratory phenomena associated with it are discovered and recorded, and the final stage in which the reasons for the occurrence of the condition are at last clearly understood. These three stages are answers to the questions What? How? and Why? When for example Addison first wrote on pernicious anæmia he answered the question "What?" and there followed a period of many years during which a mass of knowledge was acquired concerning the appearances of the patients, the various complications, the hæmatological findings, the results of gastric analysis and so on, giving us very full answers to the question "How?" But it was only when Castle at last demonstrated the effects of loss of the intrinsic factor that we had our answer to the final question "Why?" And thereupon the control of pernicious anæmia was achieved.

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remain unknown for varying periods; the establishment of standards and the definition of units may prove as useful as in the case of penicillin.

History will assign to the period between the two world wars a high place for discovery and advance in scientific knowledge. When this claim is made the minds of men turn naturally, if nowadays a little uneasily, to their triumphs in the physical sciences; yet the advances made in the biological sciences have brought, in their practical applications to the needs of man's daily life, a measure of improved health, physical well-being and consequent happiness which will bear comparison with any of his more material gains.

Some of the outstanding advances in this period have been referred to in this lecture, and there are others: the period has seen the discovery of insulin, a greatly increased knowledge of the vitamins and of their chemical nature, the discovery of the drugs of the sulphonamide type and of penicillin, of mepacrine and D.D.T., and of materials for the prevention of diphtheria and tetanus; and we have seen these discoveries bring to the diabetic an almost normal life, almost a revolution in the science of nutrition, the abolition of tetanus as the scourge of armies, protection for the individual or the community against diphtheria, and new triumphs in the prevention and treatment of infectious disease.

In some of these general advances biological standards have played a modest but useful part; and it is not unreasonable or an exaggeration to claim that this work has proved to be essential to research, and the consequent extension of our knowledge in many of those biological sciences on which the progress of medicine depends.

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"hyperpiesia" which was the name he finally employed. On the whole I feel that it is not to Allbutt nor to Huchard that the chief credit for the early recognition of hypertension should be given, but to Mahomed who, in a brilliant series of articles in the *Guy's Hospital Reports* before and after 1880, not only recorded clinical observations but confirmed these by the application of an instrument of scientific precision, Marey's sphygmograph.

By the closing years of the last century the question "What?" was answered, the recognition of the morbid process, hypertension, was accomplished. And then comes a further long interval, amounting to some forty years, during which physicians and pathologists supplied the manifold answers to the question "How?"

It is essentially in the present century that our profession has come to recognize the predominant part played by hypertension in the production of cerebral disasters and cardiac failure; the conception of malignant hypertension has emerged; the part played by hypertension in the production of retinitis, renal sclerosis, and—in spite of somewhat tardy recognition by obstetricians—in many of the greater disasters complicating pregnancy has become apparent.

A mass of knowledge has accumulated, but in spite of this much of the work has been negative in character and the researches of chemists and microscopists—so fruitful in other directions—have accumulated facts rather than the explanation. The third question, "Why?" remains unanswered, and because of this the control of hypertension has barely begun.

Nevertheless we have, in quite recent years, entered on a new epoch, and the final answers will soon be available.

If we examine the diseases most closely associated with hypertension we find that they fall into three groups, (a) nephritis, (b) certain endocrine disorders, and (c) eclampsia. Taking these in reverse order, it is clear that obstetricians have not yet got beyond the fringe of the problem, and the records of Siever and others of the promising results of caudal anaesthesia contrast with the obscurity which still lies behind the screen formed by the term "toxæmia of pregnancy". Time may show that the real linkage here is with the endocrine disturbances such as we see in Cushing's syndrome and certain adrenal tumours, in which hypertension is an outstanding feature. Nephritis remains the overwhelming association with hypertension, and just as it was nephritis which led to the first recognition of hypertension, so it is experiments connected with the kidney which have at last thrown light on essential causal factors.

EXPERIMENTAL WORK

The problem of why hypertension develops has undergone an extraordinary change since the exciting work of Goldblatt and his school. These observers showed how, by artificially diminishing the renal circulation, hypertension, of serious degree could be produced in animals without alteration of the better-known chemical constituents of the blood. Important though this work is, its greatest impetus has come from the work of Byrom and Wilson who, in a series of experiments as brilliant in conception as in technical execution, demonstrated that partial occlusion of the renal artery on one side in the rat would lead to severe hypertension, would produce changes similar to those seen in malignant hypertension in the non-clamped kidney, and, further, that subsequent removal of the clamped kidney could be followed by complete recovery of the other. How this is brought about has not yet been finally established, but it has demonstrated the extreme importance of the "vicious circle", hypertension resulting from interference with the kidney, renal damage increasing the hypertension, which must be a frequent, possibly constant, factor in the mechanism of production of this disorder.

Simultaneously with this work there have been going on other inquiries of a more chemical nature consisting of the isolation of pressor substances from the blood and tissues of normal and hypertensive subjects—both man and animal.

The first important work of this kind is perhaps that of the Swedish physiologist Tigerstedt, but it is really only much later that the experiments of I. H. Page and others have led to recognition of the real importance of these chemical phenomena. Much work has been done both here and in the Americas by Pickering, Page, Grollman and others on "Renin", "Hypertensin", "Anti:renin" and other protein substances derived from the blood plasma, sometimes from normal and sometimes from the victims of nephritis or malignant hypertension. Therapeutic results have already been claimed in experimental animals, but application to man is still awaited.

THE THIOCYANATES

One of the few practical contributions to the therapeutics of hypertension is the potassium thiocyanate treatment. No one has as yet put forward any proof as to how this substance acts. Cavinass has recently stated that it is by replacement therapy, that the blood thiocyanate is below normal in all sufferers from hypertension, but he has produced no proof of this assertion. It is perhaps this lack of scientific explanation, together with the risk of toxic effects from overdosage and the necessity for somewhat frequent blood analysis, that has made us slow in employing this treatment on a large scale. But although its action is uncertain and its use requires great care, there is no doubt at all that potassium thiocyanate does sometimes give dramatic results in properly selected cases.

Barker and his co-workers claim improvement in 50% of 246 cases observed for two to ten years. Cavinass, Kurtz and others in the U.S.A. claim a reduction of systolic blood-pressure of 15% in more than half the cases treated. It is admitted, indeed urged, that the drug is useless if the hypertension has been long established, it is further admitted that if the right blood level is not established by laboratory control serious toxic results may follow, including the onset of acute goitre as described by Potter, Foulger and others. But I cannot permit the criticism of the over-cautious or the scepticism of the ultra-scientific to divert me from the fact that this treatment is to-day the only treatment we possess to combat a disease which kills some hundred thousand people every year in England and Wales.

It is doubtful if thiocyanate therapy will survive, but it will probably disappear not on account of its uncertainties or dangers but because it will be replaced by something more effective. I believe that the new treatment, which we shall see emerge soon, will result from the researches of a group of scientists who desire the preservation of humanity rather than its destruction, who choose to devote their lives to the study of the body rather than to the perfection of the bomb.

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Dr. Clifford Wilson (*Experimental hypertension and Bright's disease*) said that, during the last ten years experimental hypertension had made a notable contribution to the understanding of Bright's disease. High blood-pressure had been produced in many animals by a variety of operations on the kidney, the common underlying factor apparently being renal ischaemia. The most significant features of experimental renal hypertension were as follows:

- (1) The increase in peripheral vascular tone which gives rise to the high blood-pressure is brought about by a chemical and not a nervous mechanism.
- (2) The ischaemic kidney may show no microscopic evidence of structural damage.
- (3) Constriction of one renal artery will give rise to persistent hypertension, particularly in the rat, so that failure of renal excretion is not the primary cause.
- (4) Increasing the load on the kidney increases the blood-pressure response.
- (5) Hypertension due to unilateral renal ischaemia gives rise to vascular and parenchymal changes in the opposite kidney and in other organs.
- (6) These closely resemble the lesions of malignant hypertension and chronic interstitial nephritis in man.
- (7) Hypertension may persist after removal of the ischaemic kidney.

Dr. Wilson discussed the work carried out by Dr. Frank Byrom and himself (1939, 1941) which was unfortunately interrupted by the war but which had been largely confirmed by other workers.

He demonstrated by lantern slides the technique of renal artery constriction in the rat and showed typical blood-pressure tracings following this procedure. Photomicrographs were shown illustrating the varieties of acute and chronic hypertensive lesions which were found in the opposite kidney, and the absence of histological changes in the ischemic kidney. That the latter was protected from the hypertension by the clip on the renal artery was indicated by the absence of medial hypertrophy in the arteries distal to the clamp. The arteries of the opposite kidney on the other hand showed great medial hypertrophy.

Application of the results of these experiments to the problems of Bright's disease had helped to clarify certain aspects which had hitherto remained obscure both to clinicians and histologists.

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(2) The malignant form of essential hypertension is established as a distinct clinical and histological entity in which renal damage is secondary to the hypertension. In the early stages it had been shown that structural changes in the kidney were minimal. Malignant nephrosclerosis was the end-result of this disorder.

(3) To the common observation that renal disease gives rise to high blood-pressure we had added the concept that high blood-pressure can produce rapidly progressive renal destruction. Taken in conjunction these premises suggested the possibility of a vicious circle in which renal ischemia leads to hypertension, and this in turn, by causing renal vascular lesions, aggravates the renal ischemia. Wilson and Byrom obtained considerable evidence that such a vicious circle developed in the experimental animal. Its operation in the human subject would explain the rapidly progressive clinical course of malignant hypertension and of other forms of hypertensive Bright's disease in their terminal stages.

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Goldblatt's work did not become widely known until 1934; immediately a great amount of work began on kidney press juices, extracts, and autolysates. Tigerstedt and Bergmann in 1898 had shown the presence of a heat labile non-dialysable pressor compound peculiar to extracts of renal cortex. The purification of renin, and the way in which it carries out its pressor action, were arrived at mainly by two groups of workers, one in North and the other in South America; they used different terminology. [I shall use the South American terminology, adding the North American in parentheses.]

Renin has been shown to be an enzyme, liberated from the renal cortex into the blood-stream where it acts on a blood globulin, hypertensinogen (angiotonin activator), to form the one pressor compound of the renin system, hypertensin (angiotonin).

Renin.—The enzymatic action of renin is proteolytic, but it acts only on hypertensinogen (angiotonin activator) and not on other proteins. This is known because pepsin can replace renin in the conversion of hypertensinogen (angiotonin activator) to a pressor compound. Renin is an antigen, but the development of a high precipitin titre does not reduce its physiological action. Renin also shows species specificity: human renin will act on the hypertensinogen of all mammals, but that of other mammals will not act on human hypertensinogen (angiotonin activator). This species specificity has been used in the development of the biochemical methods for the assay of renin.

The site, either of renin storage or of its formation, has been localized to the proximal convoluted tubules. It is only excreted in the urine after very large doses.

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Section for the Study of Disease in Children

President—Professor NORMAN B. CAPON, M.D.

[October 26, 1945]

The Training of Clinical Teachers

PRESIDENT'S ADDRESS

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Those who have taken a special interest in the subject of medical education will be aware that there have been occasional references, in recent years, to the question of the teachers themselves—and especially to their fitness and competence to carry out their educational duties.

By way of explanation I should say that I am speaking of *all* clinical teachers—whether they specialize in medicine, surgery, paediatrics, dermatology, ophthalmology, &c., because I am concerned with education in general and teaching methods in general, rather than with the content of the subject taught. And here let me interpose the observation that paediatricians have adhered more closely to the tenets and discipline of the art and science of medicine than any of the specialists; and this is to be expected because paediatrics is in fact general medicine during a particular age-period. Indeed, I would go further, and claim with some assurance that the contribution made to general medicine by paediatricians has been considerable; and I believe that the conditions, both personal and professional, of our work place us in an unusually favourable position for promoting improvements in basic medical education. To do this would be a service well worthy of the great traditions which we have inherited from men like West, Cheadle, Barlow and Still.

Clinical teachers have in the past been inclined to blame the preclinical teachers when students come to the wards without any adequate acquaintance with the general principles of science. There is probably some foundation in this complaint, but it does not exonerate clinical teachers from a share of responsibility if they themselves perpetuate the error which they impute to their preclinical colleagues. Perhaps if we put our "clinical" house into better order we may encourage others to do likewise.

After this brief introduction I shall refer to some of the statements which have been made regarding clinical teachers. The Goodenough Report, concerned with "the

hypertension and essential hypertension, but its responsibility for the hypertension of renal ischaemia cannot be said to have been clearly established by the usual methods of assay, and further work is needed to establish whether it is in fact the causative, or the only causal agent. The results of slow renin infusion experiments give cause for some doubt as to whether a sustained increase of renin secretion could produce prolonged hypertension; for instance, Hill and Pickering found that by slow infusion of renin into normal anaesthetized rabbits it was difficult to maintain a rise of arterial pressure of more than 30 mm.Hg for four hours, faster injections gave a larger temporary rise followed by a fall. After infusions have been continued for some time, tachyphylaxis develops.

Huidibro and Braun-Menendez were able to demonstrate that considerable lowering of the blood-pressure in normal unanaesthetized dogs as a result of trauma or haemorrhage was immediately followed by the liberation of renin from the kidneys into the blood-stream. Although anoxaemia did not prevent the secretion of renin under these conditions, such a sudden liberation of renin into the blood-stream could not be produced by anoxaemia alone.

The properties of renin would make it appear possible that renin is normally concerned with the regulation rather than the maintenance of normal blood-pressure, and the development of tachyphylaxis gives cause for doubt whether excess of renin can be responsible for a persistently elevated blood-pressure.

There is little doubt that following the production of a reduced blood supply to a kidney a chemical agent is secreted which produces a pathological state indistinguishable from essential hypertension. The initial cause for the liberation of this chemical agent in the disease itself and the nature of the chemical agent have not yet been clearly demonstrated.

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organization of Medical Schools, particularly in regard to facilities for clinical teaching and research," contained the following observation (p. 41, para. 15): "In the past too little attention has been paid to the training of teachers of medical students"; and in the same paragraph of the Report one reads: "Help and guidance in the acquisition of skill in the difficult and subtle art of teaching will enable an intending teacher to avoid much fruitless expenditure of time and effort in preparing himself for his important duties and will greatly assist him to make the most effective use of his personal qualities."

The Report of the Planning Committee of the Royal College of Physicians of London (1944) stated on p. 8: "We wish to draw attention to the importance of quality in teaching" but it does not indicate how that quality is to be secured and maintained, except by a reference to the value of the tutorial method in teaching.

Sir Thomas Lewis [1] in his "Reflections upon Reform in Medical Education" referred to the differences between vocational and theoretical training, and pleaded that students should be encouraged to develop a more thoughtful and critical outlook; in his view the whole-time teachers of the future should provide the cultural (as distinct from technical) training of the students, as a supplement to that given by clinical teachers, who would be mainly responsible for "vocational" tuition.

The B.M.A. Committee [2] which was invited to prepare a memorandum of evidence for the Goodenough Committee stated: "Students should be taught the fundamental principles of health and disease rather than the diagnosis and treatment of separate diseases. A thorough knowledge of fundamental principles will produce a more understanding practitioner who will be able readily to absorb the advances in medical knowledge and technique as they occur during his career. Many practitioners at the present time find difficulty in keeping abreast of modern medical progress because they did not acquire a sufficient foundation in their student days." This memorandum evidently assumes that we teachers are competent to provide the type of basic education which it advocates.

I think it is possible that there is general agreement regarding the wisdom contained in these various observations—at all events in so far as broad principles are concerned. But we must consider their practical implications. How, in fact, are we to ensure that while the student learns what is essential of factual knowledge, he shall at the same time be given a real education—a basis upon which he can continue to build from his own experience because he understands general principles? It is not enough for us to recommend a modification of the subjects which comprise his curriculum, or a change of the type of clinical material demonstrated to him (substituting patients with common disorders for those suffering with rare diseases), nor to be satisfied with a pious hope that the lecturer, busily engaged in a place devoted to the injured and sick, shall remember to remind the students that some people, at any rate, are healthy, though they may require advice if they are to preserve that health. These and other such recommendations may be wise and, if put into practice, may constitute valuable reforms; but they are the individual facets of one stone, the limbs and separate parts of one body, and it is to the heart of that body that we must turn our minds. For it is from the teacher that the life-blood of education flows. In this regard I cannot do better than quote from the article on Education which is to be found in the *Encyclopædia Britannica*:

"All education is effected through the experiences of the educated, but it does not follow that all experiences are educative; this depends upon whether its form has been arranged by those who are concerned with the training of him whose experience it is."

And again:

"The goodness or badness of an education will be relative to the virtue, wisdom and intelligence of the educator. It is good only when it aims at the right kind of product, and when the means it adopts are well adapted to secure the intended result and are applied intelligently, consistently and persistently."

We clinical teachers may reasonably claim to be experienced and competent practitioners of medicine; can we claim also that we are trained educators? I submit that, with a few exceptions—the born teachers, or the men of unusual vision, or those who, in spite of the busy calls of professional life, have made a special study of their teaching duties—we cannot make this claim. How, then, are we to ensure that our successors in clinical teaching shall be more competent? or, at least, shall have the opportunities to develop greater competence in this direction? Clearly this is a matter for the Universities themselves—and not, I would submit, for all Universities to undertake initially; an experiment might be started in one or two centres where there may happen to be a group of enthusiastic teachers. The plan, as I see it at present, might be as follows: In a given University a small group of senior teachers, aided by one or two preclinical teachers and

the Professor of Education, would hold preliminary discussions and would arrange a vacation course, perhaps three weeks in duration, for junior clinical teachers—e.g. registrars and assistant physicians, surgeons and specialists. The number of those taking the course should be restricted, perhaps to fifteen; and some at least of them should come from other centres in order that the discussions, which would form an important feature of the course, should represent the views and habits of different schools. The following aspects of medical education would require treatment, partly as lectures, partly as discussions and in some cases by demonstration:

- (1) The meaning of education, with some reference to educational methods in general.
- (2) The scope and aims of medical education with special reference to (a) undergraduates; (b) graduates, including general practitioners, specialists and consultants, research workers, public health workers and administrators.
- (3) The historical approach in medical education: and the value of non-medical literature.
- (4) The artistic (or humanistic) approach.
- (5) The scientific method, with special reference to experimental inquiry. Its clinical application, including the technique of medical examination.
- (6) Elementary logic, including critical analysis of evidence and assessment of values. Statistics.
- (7) The technique of clinical teaching.
- (8) The place of psychology in teaching.
- (9) The use of medical libraries.
- (10) The preparation of scientific reports and papers.

[Professor Capon then commented upon some of these topics and indicated, in greater detail, what they comprised. He also offered for consideration the following list of books and papers which would be of interest to those studying the subject.

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|--|---|
| (1) Herbert Spencer | Education. |
| (2) Sir Thomas Browne | Religio Medici. |
| (3) Sir Wilfred Trotter | Collected Papers. |
| (4) Sir Richard Livingstone | Plato and Modern Education (Rede Lecture). |
| (5) Bruce Truscot | Red Brick University. |
| (6) John Gregory | Duties and Qualifications of a Physician. |
| (7) A. G. Hughes and E. H. Hughes | Learning and Teaching. |
| (8) Francis Thompson | Essay on Shelley. |
| (9) Report of the Commission (1932) on | Medical Education. |
| (10) Sir Edward Mellanby | The State and Medical Research (Harveian Oration). |
| (11) Sir Wilson Jameson | War and the Advancement of Social Medicine (Harveian Oration). |
| (12) White House Conference Report on | Pædiatric Education and Practice. |
| (13) Writings of Sir William Osler. | |
| (14) A. G. Gibson | The Physician's Art. |
| (15) Charles West | The Profession of Medicine. |
| (16) Sir Henry Dale | Some Epochs in Medical Research (Harveian Oration). |
| (17) Sir George Newman | Thomas Sydenham, Reformer of English Medicine. |
| (18) Major Greenwood | Authority in Medicine (Linacre Lecture). |
| (19) Sir Frederick Still | History of Pædiatrics. |
| (20) Sir Thomas Lewis | Clinical Science (Harveian Lecture). Exercises in Human Physiology. |
| (21) Francis Bacon | Novum Organon. |
| (22) M. Arthus | Philosophy of Scientific Investigation. |
| (23) Henry Cohen | The Nature, Method and Purpose of Diagnosis (Skinner Lecture). |
| (24) Alan Gregg | The Furtherance of Medical Research (Terry Lecture). |
| (25) M. R. Cohen and E. Nagel | Introduction to Logic and Scientific Method. |
| (26) W. S. Jevons | Elementary Lessons in Logic. |
| (27) A. Wolf | Textbook of Logic. |
| (28) R. H. Thouless | Straight and Crooked Thinking. |
| (29) A. N. Whitehead | Modes of Thought. Adventures of Ideas. |
| (30) Susan Stebbing | Thinking to Some Purpose (Pelican Series). |
| (31) Oxford University Press | Rules for Compositors and Readers.] |

organization of Medical Schools, particularly in regard to facilities for clinical teaching and research," contained the following observation (p. 41, para. 15): "In the past too little attention has been paid to the training of teachers of medical students"; and in the same paragraph of the Report one reads: "Help and guidance in the acquisition of skill in the difficult and subtle art of teaching will enable an intending teacher to avoid much fruitless expenditure of time and effort in preparing himself for his important duties and will greatly assist him to make the most effective use of his personal qualities."

The Report of the Planning Committee of the Royal College of Physicians of London (1944) stated on p. 8: "We wish to draw attention to the importance of quality in teaching" but it does not indicate how that quality is to be secured and maintained, except by a reference to the value of the tutorial method in teaching.

Sir Thomas Lewis [1] in his "Reflections upon Reform in Medical Education" referred to the differences between vocational and theoretical training, and pleaded that students should be encouraged to develop a more thoughtful and critical outlook; in his view the whole-time teachers of the future should provide the cultural (as distinct from technical) training of the students, as a supplement to that given by clinical teachers, who would be mainly responsible for "vocational" tuition.

The B.M.A. Committee [2] which was invited to prepare a memorandum of evidence for the Goodenough Committee stated: "Students should be taught the fundamental principles of health and disease rather than the diagnosis and treatment of separate diseases. A thorough knowledge of fundamental principles will produce a more understanding practitioner who will be able readily to absorb the advances in medical knowledge and technique as they occur during his career. Many practitioners at the present time find difficulty in keeping abreast of modern medical progress because they did not acquire a sufficient foundation in their student days." This memorandum evidently assumes that we teachers are competent to provide the type of basic education which it advocates.

I think it is possible that there is general agreement regarding the wisdom contained in these various observations—at all events in so far as broad principles are concerned. But we must consider their practical implications. How, in fact, are we to ensure that while the student learns what is essential of factual knowledge, he shall at the same time be given a real education—a basis upon which he can continue to build from his own experience because he understands general principles? It is not enough for us to recommend a modification of the subjects which comprise his curriculum, or a change of the type of clinical material demonstrated to him (substituting patients with common disorders for those suffering with rare diseases), nor to be satisfied with a pious hope that the lecturer, busily engaged in a place devoted to the injured and sick, shall remember to remind the students that some people, at any rate, are healthy, though they may require advice if they are to preserve that health. These and other such recommendations may be wise and, if put into practice, may constitute valuable reforms: but they are the individual facets of one stone, the limbs and separate parts of one body, and it is to the heart of that body that we must turn our minds. For it is from the teacher that the life-blood of education flows. In this regard I cannot do better than quote from the article on Education which is to be found in the *Encyclopædia Britannica*:

"All education is effected through the experiences of the educated, but it does not follow that all experiences are educative; this depends upon whether its form has been arranged by those who are concerned with the training of him whose experience it is."

And again:

"The goodness or badness of an education will be relative to the virtue, wisdom and intelligence of the educator. It is good only when it aims at the right kind of product, and when the means it adopts are well adapted to secure the intended result and are applied intelligently, consistently and persistently."

We clinical teachers may reasonably claim to be experienced and competent practitioners of medicine; can we claim also that we are trained educators? I submit that, with a few exceptions—the born teachers, or the men of unusual vision, or those who, in spite of the busy calls of professional life, have made a special study of their teaching duties—we cannot make this claim. How, then, are we to ensure that our successors in clinical teaching shall be more competent? or, at least, shall have the opportunities to develop greater competence in this direction? Clearly this is a matter for the Universities themselves—and not, I would submit, for all Universities to undertake initially; an experiment might be started in one or two centres where there may happen to be a group of enthusiastic teachers. The plan, as I see it at present, might be as follows: In a given University a small group of senior teachers, aided by one or two preclinical teachers and

of the specialism which rightly claims him as a master and wrongly tempts him to become its slave.

Fourthly, can a teacher learn anything worth knowing of medical education in a three weeks' vacation course? I do not claim that such a course can do more than present a view-point, inspire interest and suggest a practical curriculum for study. Here is the first stone of an educational foundation upon which the teacher can build; his proficiency will grow with practice. But he will be stimulated to ask of himself three all-important questions: *Why* am I to teach? *What* am I to teach? and *How* am I to teach? and to seek intelligent answers to these questions. There must be no interference with the liberty and originality of the teacher who, in accepting the role of educationalist, takes upon himself a burden of responsibility no less heavy than that of clinician. But are we being fair to him in denying him the opportunity of organized study?

REFERENCES

- 1 LEWIS, Sir THOMAS (1944) *Lancet* (i), 619, 649 and 685.
- 2 *British Medical Journal* (1943) (i), 702, Interdepartmental Comm. on Med. Schools.

Sir Adolphe Abrahams: I am dubious of the possibility of systematically educating teachers, I mean, of course, of clinical medicine. The application of pedagogy may well be successful in respect to general education but medicine seems to me to be in an isolated category. So much depends on the teacher's personality. One man may be completely didactic, another may adopt the Socratic method, and a third may say exceedingly little and yet create an atmosphere from which his followers appear to absorb instruction. And all may be equally successful yet fail miserably if called upon to employ a style or method foreign to their individuality.

Moreover one has to remember that the teaching directed to assist students to pass their examinations and that which prepares them for the real business of their professional lives are by no means the same thing. An exceptional man may combine the two functions but it seems unfortunate that the majority of teachers are far too much influenced by the problem of Queen Square and similar ordeals. It is often urged that some place should be found in the curriculum for a course of instruction by a general practitioner. That students could learn much from a practitioner of experience needs no emphasis, so for that matter can consultants. But although a course of lectures might comprehend certain technicalities that are features of practice, I think that little of real value can be communicated by word of mouth. The opportunity of a sort of apprenticeship in order to study the methods would provide a valuable experience but such an arrangement could hardly be practicable.

I deprecate the growing tendency to delegate the teaching of undergraduates to men of the registrar class. These, however brilliant academically, have not the maturity to inculcate the fundamentals. A common error is to confuse education with instruction. Students are only too ready to welcome spoon-feeding but teachers are not required to save them from taking trouble although they may direct them in the way of taking trouble and perhaps save them from taking unnecessary trouble. There is a further great advantage in the status of the senior, the prestige which is naturally associated with a position on the Honorary Staff adds enormously to the value of his *ex cathedra* pronouncements.

A final word about postgraduate teaching. Whilst in my opinion undergraduate teaching in this country is the best in the world, the quality of postgraduate instruction calls for considerable improvement. It is not difficult for anyone who has studied on the Continent to supply reasons for our comparative inferiority but doubtless this aspect of medical education will receive special attention by those who will be responsible for organizing the future.

Sir Ernest Rock Carling said he thought a great deal could be done by a faculty of pedagogy giving instruction in method, towards turning the young clinician into an effective teacher.

The clinical teacher's education should begin with the humanities; not necessarily Greek and Latin classics. A competent knowledge of a foreign language giving access to a great literature was what was wanted. To make for clarity in speaking, as in writing, some instruction in linguistics was desirable. A teacher should understand the true function of words and how they should be adapted to the level of conversation.

At some period after qualification, travel to and work in other clinics at home or abroad was very valuable. Thereafter visits in the company of colleagues gave exceptional opportunities for heart to heart exchange of experience. Without them it was difficult to maintain a standard of self-judgment.

It was not to be expected that all men should do fruitful research, but a period served in a research department was valuable as an initiation into scientific method and way of thought. At least it taught accuracy of observation and something of the value of statistics. The use of the library, books and records, should be learnt by the production of contributions to the literature. The memory should not be taxed by attempts to cover the whole field, but full factual acquaintance with all the data in some specialized part should be at command.

It will be apparent that the subject matter of the course is divisible into two sections: (a) basic education and (b) the technique of teaching. The former is the more important because it concerns itself with general principles, and clinical teachers who are prepared to devote some time to studying this aspect of their duties will be the better able to ensure that their students are in fact educated as well as vocationally equipped. In parenthesis I should state that no part of the tuition given to teachers is intended to be directly transmitted to students, and I stress this because it would be a mistake to believe that I am advocating that students, at all events during their clinical years, should find their curriculum made still more congested by the inclusion of lectures on logic and kindred subjects.

Perhaps I may best expand the theme of this address by considering some of the criticisms or objections which are likely to be put forward. First, it may be argued that junior clinical teachers have little time and sometimes little inclination for work which is not strictly technical or vocational. Lack of time is a defect which is likely to be corrected by a change in policy regarding teaching duties, for which little if any direct payment has been made in the past. Teaching, and preparation for teaching, takes time and it is very probable that this service will be put on a proper financial basis in the near future. We shall, I think, all agree that the best medical education cannot be provided by clinicians who must, by force of circumstances, regard their teaching duties as subsidiary to their routine professional service. At present it is true to say that most clinical teachers have scarcely time even to think; but the wisdom of the medical educator no less than that of the scribe cometh by opportunities of leisure, and I believe that one of the strongest arguments in favour of a vacation course such as I advocate will be found in the inspiration and renewed enthusiasm which it is likely to bring to junior clinicians.

As for lack of inclination I can only state my own experience of young clinical teachers, which is that they are most anxious to learn and to improve their competence as teachers.

Secondly, it may be argued that there are at present no clinical teachers, even among the seniors, who are equipped for the difficult task of conducting a course on the general lines suggested, and that the work would therefore have to be "farmed out" to non-medical educationists, scientists and philosophers whose ignorance of medicine would be a fatal handicap. It is my view that if the suggested course is to be effective in a practical way it must be conducted mainly by practising clinicians, perhaps with the advice and assistance of non-medical specialists; and I would go further and plead that it would be mistaken policy to leave this basic education entirely in the hands of clinicians whose experience is largely, if not solely, confined to hospital practice. If we accept, as I think we must, that practising clinicians capable of taking charge of such a course are at present few in number, the fact must be regarded as a strong argument in favour of correcting such a deficiency in the future. A start must be made; it will be pioneer work, with all the thrill and excitement of a new venture, and I am confident that its ultimate success will give new point to the conception that the intellectual function cannot afford to stand still, but must be growing and developing if it is to retain full health and vigour.

Thirdly, the view has been put forward, in discussion, that teachers are born, and cannot be made; and that if a clinician is really proficient in his professional work and "knows his stuff", the student learns both by precept and example. Indeed, the fear has been expressed that a clinician's skill in practice and his ability in handling patients may be jeopardized by overmuch attention to theory and rationalization. There is some substance in this argument, for we must all know clinicians of the "research" type whose critical scientific attitude has resulted in a certain diffidence of manner and flabbiness of authority in the sphere of human relationships which has been detrimental to their success in therapeutics. I give place to no one in my respect for the really first-class practising clinician—whether he be general practitioner or specialist; to me he represents the highest degree of excellence that has been attained in our profession. But we do him less than justice if we assume that by an active effort to broaden the basis of his knowledge and cultivate wisdom he will thereby reduce his technical efficiency. And it is not sufficient that the teacher should "know his vocational stuff", though that is, of course, a *sine qua non*; he must possess intellectual poise and expansiveness of mind if he is to guide students wisely through the narrow and complicated pathways

of the specialism which rightly claims him as a master and wrongly tempts him to become its slave.

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For the rest, "apprenticeship" was the real substance of the education needed. His own plan with a chief assistant was to take him for a year, during which he laid himself out to teach the prospective surgeon all he knew. If satisfied, he took him for a second year, during which he acted as assistant to the young man. At the end of that year, if convinced there were the makings of a surgeon, he kept him on for a third year, with full responsibility, acting himself merely as consultant. With the close of that year he felt he could recommend him to any clinic that would accept him to complete his education.

Dr. Ffrangcon Roberts: Having long felt that medical education should be approached from the point of view of education I heartily welcome the President's scheme for the training of teachers and hope he will be enabled to put it into effect. The faults in medical education, the overcrowding of the curriculum, the excess of factual information and the absence of training in logical thought have been stated so often in recent years that their repetition makes wearisome reading. The problem is no longer what is wrong, but why, when everyone knows what is wrong, no remedy can be found. I believe that the President has pointed one way to the solution.

My experience as Manager of three Council Schools has taught me that the problem is by no means confined to medicine. Leading educationists are fully aware of the perpetual struggle which the observational and naturalistic approach perpetually wages against the tyranny of the textbooks and stereotyped class instruction. Nevertheless it is to them a matter of constant study and experiment, and one cannot help contrasting their enthusiasm with the stagnation and inertia which beset medical education. There are many outside our profession to whom we might listen with profit.

As long ago as 1918 Sir George Newman pointed out that medical education had not kept pace with the advance in medicine. The reason of course is that medicine is studied but medical education is not studied. We shall make no progress until we realize that the presentation of the curious combination of science and art of which medicine is composed is a subject which requires intensive training and study. One way to keep interest alive in this matter would be the formation of an Education Section of this Society.

Section of Anæsthetics

President—GEORGE EDWARDS, M.R.C.S., D.A.

[November 2, 1945]

Tribromethyl Alcohol (Avertin, Bromethol), 1928-1945

PRESIDENT'S ADDRESS

By GEORGE EDWARDS, M.R.C.S., D.A.

TRIBROMETHYL ALCOHOL is more commonly known as avertin. It is also known as bromethol in this country and as bromethanol in the United States. I propose to use these terms interchangeably as may be convenient.

Starting with a few tentative cases in 1928, the use of avertin became popular and widespread and only with the later introduction of more convenient drugs and methods has that popularity waned. From my own figures I find that in 1936 20% of hospital patients and 65% nursing home cases were given avertin. During the last twelve months I find that less than 5% of hospital cases and under 10% of private cases have had this drug, and my colleagues assure me that their experience is similar to my own.

In 1927 notices began to appear in the medical papers describing the use in Germany of a new anæsthetic agent named by its makers "Avertin" and numbered "E107". This new drug, it appeared, was the answer to all anæsthetic problems. The patient went peacefully to sleep in bed half an hour beforehand, was completely and safely anæsthetized, and woke up some two or three hours later, with no sickness, no headache and very little pain. The only bar to its use was said to be disease of the rectum, colon, kidney or liver. A quantity of this new drug was obtained for trial here, and was distributed by the Anæsthetics Committee, which had been set up jointly by the Medical Research Council and the Council of this Section of your Society. Some of the avertin to be tried was sent to Dr. Shipway at Guy's Hospital and some to Dr. Blomfield at St. George's. As resident anæsthetist to the latter, it fell to my lot to discover all that there was to be known about the preparation of the drug for use, and to make arrangements for trying it out.

It appeared that avertin was tribromethyl-alcohol, a white crystalline solid, soluble in water to something over 3% at 40° C. If such a solution was given rectally in quantity equivalent to 0.1 gramme per kilo of body-weight, then absorption of the drug would gradually produce anæsthesia, reaching its greatest depth in thirty to forty minutes and lasting up to two hours. The other salient point was that the solution must be freshly prepared and that it must be tested by the addition of Congo-red solution prior to use. If a blue colour appeared, or, indeed, anything but bright orange-red, then the solution must be discarded as dangerous. It seemed that a decomposition into dibromacetaldehyde and hydrobromic acid might take place—the former was dangerous and the latter was indicated by the change of colour in the Congo-red. The advantages held out for this form of anæsthesia were not only the preliminary narcosis and the peaceful awakening, but also the absence of sickness and of post-operative chest troubles. Rectal anæsthesia was by no means new: ether-oil was well known and paraldehyde had been largely used but neither had become popular.

All that now remained was to use the avertin. One of the surgeons expressed his willingness to co-operate, or, rather, he agreed not to object. We asked to be told when there was a simple operation to be performed on a healthy subject. It came in the form of an exploration of the floor of the mouth in a young woman suffering from salivary calculus. The operation took place on March 20, 1928, and, as far as I can discover, this was the first occasion on which tribromethyl alcohol was used in this country. I wish to recount the case in some detail, solely to point out the differences between what we then did and anticipated, and what we now consider to be reasonable.

We started off with a rectal washout accompanied by the hypodermic injection of one-third of a grain of omnopon. 4.8 grammes of avertin crystals, representing 0.1 per kilo of body-weight, were dissolved in 160 c.c. of distilled water, making a 3% solution. That sounds a simple enough business but in fact it meant a great deal of shaking and was wearisome and tedious. The solution, finally achieved, was found to be acid-free on addition of the Congo-red and was run into the patient's bowel, taking seven minutes. With the idea of assisting in its retention, the catheter was removed and a vaseline-wool

plug was placed in position. The patient rapidly dozed off, and in fourteen minutes it was observed that the conjunctival reflex was absent and the corneal reflex was faint. In three more minutes the corneal reflex had also gone and there was no response to pinching the skin of the thigh. The surgeon was invited to proceed and his incision into the floor of the mouth was made twenty-three minutes from the time we had begun the injection of the avertin. No objections were raised by the patient until the surgeon delved deeply into the sublingual tissues. This brought a groan. Shortly afterwards, there was a cough. The actual operation lasted seventeen minutes and the patient was returned to the ward with her corneal reflex still absent. A thorough rectal washout was started at once. Recovery and convalescence were uneventful.

On the whole, we were very pleased. The avertin had produced almost complete anaesthesia, nothing untoward had occurred and the patient had certainly had a much easier time than was the usual lot in those days when premedication consisted of atropine only, and when the porters who brought a case from the ward stayed in the anaesthetic room to hold it down during induction. We were unable to get any subjective views on the matter; not only had the patient never been anaesthetized before, but we had taken every precaution to prevent her from knowing that anything unusual was happening.

No doubt various items in the account of this case have caused you to raise your mental eyebrows. I would ask you to remember that all this happened a long time ago—seventeen years and a half—in what has been unkindly referred to as the "age of dark anaesthesia when 'closed ether' was still popular". My own comments on this case are nine in number, and I will try to deal with them as briefly as possible.

(1) There was a pre-premedication with omnopon. This helped in the anaesthesia; but, as was later remarked by Sir Francis Shipway, the same result could be attained with less respiratory depression either by a small amount of additional inhalation anaesthetic, or even by a relatively slight increase in the avertin dosage.

(2) The drug was supplied in crystals and had to be weighed out and dissolved. In the following year (1929) "avertin fluid", as we know it to-day, was available, and preparation of the dilute solution became a comparatively simple matter.

(3) A 3% solution was used. The usual strength is now 2½%: the volume is not unduly increased, the mixing is easier, and there is less danger of the avertin crystallizing out.

(4) A rectal washout was given just before the administration. This was an unnecessarily vigorous proceeding. In any case, it was ill-timed; if the bowel is emptied by washout or by enema, it should be allowed to rest for an hour or two before being expected to retain a further injection.

(5) A cotton-wool plug was used lest the fluid be returned. In spite of the use of such plugs—or more probably because of their irritation—we used occasionally to lose our avertin in the bed sheets. It was soon evident that greater safety was achieved either by gently withdrawing the catheter or, even better, by leaving it in situ carefully clipped.

(6) The depth of anaesthesia was tested by examining the conjunctival and corneal reflexes. Apart from the fact that poking one's finger into a patient's eye is strongly to be deprecated in any circumstances, it was very obvious that the narcosis produced by avertin was against the ordinary run of things. The patient might have lost his ocular reflexes, but he could still kick back when attacked by the surgeon or, as in this particular instance, could cough when blood trickled into the larynx.

(7) Full surgical anaesthesia was expected with this standard dose. We did not anticipate any need for supplementary inhalation.

(8) Such completeness was in point of fact not attained. The patient was sensible enough to retain her laryngeal reflex and to protect herself against the passage of any foreign material into her trachea.

(9) A rectal washout was given at the end of the operation—over an hour from the time of starting the avertin injection. This was useless: it would neither prevent further absorption, nor assist in elimination.

Such, then, was the first case. The next was a gastrectomy, and went very happily. Herniotomies and appendicectomies followed satisfactorily. An attempt was made to get complete anaesthesia for the removal of a large thyroid cyst. The omnopon was increased to two-thirds of a grain, and the avertin was at the rate of 0.125 gramme per kilo. The resulting anaesthesia was complete and satisfactory, but, unfortunately, permanent, the patient dying some twenty hours later without recovering consciousness. By this time, it was evident that only very small doses of inhalation anaesthetic were required to complete a partial avertin anaesthesia, and it was decided henceforth to use only the standard dose of avertin—or, in other words, to seek for basal narcosis rather than complete anaesthesia.

On March 16, 1929, the *Lancet* (i), 546, published a paper by Drs. Blomfield and Shipway. It bore the title, "The Use of Avertin for Anæsthesia" and summed up the results not only of their own cases, but also the observations made by Mr. Basil Hughes of Bradford, Mr. F. J. Morrin of Dublin and Dr. F. P. de Caux. The paper was published at the request of the Anæsthetics Committee which had distributed the samples. In its penultimate paragraph was a verdict, which ran: "We consider avertin to be a valuable addition to the drugs at the disposal of the anæsthetist and that if it is used with due care and moderation its advantages can be taken advantage of with perfect safety."

This cautious approval seems to be slightly complicated in its wording but it provided the "Go-ahead" signal, and avertin was put on general sale to the profession. The manufacturers, however, were cautious too. They labelled it, "The Basal Narcotic", indicating that its true use was preliminary to rather than productive of anæsthesia.

From 1930 onwards there appeared in the medical papers almost innumerable articles, annotations and letters on the subject of avertin narcosis. It was used in conjunction with local anæsthetics, with spinals, and with every kind of general anæsthetic, even including chloroform. All users were unanimous in its praise, and reading back over the literature, one begins to feel that a competitive game was being played as to who could use bromethanol in the youngest, the oldest, the most obese or the most dangerously ill patient. It is not needful to refer to the majority of these articles, but certain of them were of particular importance.

Very much to the point was the paper by W. P. Kennedy on "Effective Counteraction of Avertin Narcosis". This was a timely document for, although it was abundantly clear that avertin narcosis in routine dosage was safe for normal patients, restorative measures then known were not very effective in dealing with the respiratory and circulatory depression which occurred when a comparative overdose chanced to be given. Washing out the rectum was of little use unless the untoward symptoms were observed before all the avertin had been absorbed—and this would only occur when a gross overdose had been given. The only thing to do was to keep the patient going and wait for gradual recovery. Carbon-dioxide-oxygen and ephedrine were found to help, and varying views were expressed as to the value of thyroxin. The way in which thyrotoxic patients effectively disposed of normal and larger doses of avertin immediately suggested that an artificial thyrotoxicosis, by the giving of the hormone, should be an effective restorative measure. Pribram published in Germany in 1929 a paper stating that intravenous thyroxin was effective. The particular cases he describes are not very convincing proofs of its value, and other observers failed to find it of use. Indeed, one writer found that the thyroxin had to be given for some days before becoming effective! This was not much help.

Kennedy, however, followed up and confirmed an assertion made in Germany by Killian that avertin narcosis could be quickly and effectively counteracted by the intramuscular or, better, intravenous injection of pyridine beta-carboxylic acid diethylamide. This drug is now our old friend coramine, and our rechristened colleague nikethamide. Kennedy used this stimulant on avertinized cases in Dr. James Young's gynæcological clinic in Edinburgh, and was able to report very favourably on its value, saying that "Coramine is an effective agent in counteracting and interrupting the cardio-respiratory depression of avertin anæsthesia, which occasionally reaches a point where active measures are necessary to overcome it".

Though there was no doubt that with careful choice of case and with reasonable administration, avertin overdosage was an unlikely event, we now had the moral support of knowing that an effective stimulant was at hand.

From the very beginning it had been suspected that tribromethyl alcohol, being a halogen compound, would be a potential danger to the liver. Unfortunately, pharmacological investigations did not produce very clear-cut results; it was difficult to decide how much importance was to be attached to the various tests of liver function. Wesley Bourne of Montreal experimented on dogs and showed that "repeated administration in normal dogs produced only a mild parenchymatous degeneration of the liver and kidneys: fatty changes in the liver occurred occasionally; when they did, they were very slight". In 1933, however, in collaboration with L. H. McKim, Bourne reported on a patient who had had twenty-two avertinizations within a period of ten weeks. The unfortunate man had had a severe infection of the leg following a road accident, and had needed a series of painful dressings. Bourne investigated the liver function by bromsulphalein dye retention tests, by observing the pigment metabolism, and by determining sugar tolerance. His report was that "even after the twenty-two doses there was no retention of the dye, which compares very favourably with the action of one dose of this or any other anæsthetic agent". Such changes in pigment excretion and of the blood-sugar concentration as were observed were not cumulative, were referable to the patient's general condition, and were not observable at the time of the twenty-second administration.

Meanwhile, anæsthetists in general were seeing but little evidence of hepatic damage due to or aggravated by avertin. In the first paper, Blomfield and Shipway record an instance of the drug having been used successfully in a jaundiced patient operated on for gall-stones. In 1932 H. K. Ashworth reported three successful cases of avertinization in the presence of definite hepatic damage. By 1935 Sir F. Shipway was able to record 1,600 cases of avertin administration, in only two of which had there been any evidence of liver disturbance. Both these cases had had avertin plus ether, and both had shown a slight but transient jaundice post-operatively; one was a child with a long history of acidosis, and the other an adult who at operation was seen to have a cirrhotic liver. These two cases could hardly be regarded as an indictment of avertin, and from the same series Sir Francis was able to quote two cases of very ill and jaundiced patients who made uninterrupted recoveries even though they were given this narcotic.

On both sides, then, the pharmacological and the clinical, it seemed that avertin was harmless to the liver and, further, that even the damaged liver was no contra-indication to its use. Nevertheless Rabinovitch of Montreal, in discussing Bourne's findings, says, "Avertin should be used with great care in the presence of an obviously damaged liver (jaundice, &c.)", whilst Shipway concludes that avertin may be administered in a dose "suitably adjusted" to patients suffering from jaundice, cirrhosis or other forms of liver damage.

Now in real point of fact, these apparent permissions amount to practical prohibition. To use avertin "with care" or in "suitably adjusted doses" requires more detailed knowledge of pharmacology in general, and of the individual patient's pathology in particular, than falls to the lot of the common or garden administrator of anæsthetics. What is of value is the realization: (a) That avertin used in the normal way is unlikely to damage a healthy liver, and (b) that if there is any suspicion of interference with hepatic function, avertin should be avoided, notwithstanding the many recorded cases in which it has been safely used in the presence of liver damage.

Kidney function and the use of tribromethyl alcohol are, of course, intimately related. Again, there are two aspects of the problem: the excretion of the detoxicated drug, and the effect of the drug on normal renal activity. F. B. Parsons of Cambridge investigated the excretion of the drug in rabbits, and was able to publish a paper on his findings as early as October 1929. This was followed by similar investigations by other workers, and very little was agreed upon other than that half or more of the combined brom-ethanol was excreted during the first day after injection, and that the remainder took several days. Much more positive were the findings of E. N. Pitt of Guy's Hospital, who investigated the effect of avertin on human renal function. This work was undertaken at the request of the Joint Anæsthetics Committee which we have already mentioned and the findings were published in the *Lancet* of March 30, 1935. In his conclusions, Pitt states that: "In spite of the conditions which tend to hamper renal function during anæsthesia, nitrogen excretion is actually very little upset by the volatile anæsthetics and less so by avertin."

Meanwhile, the value of avertin narcosis in cases of thyrotoxicosis had been more and more appreciated. From the beginning it was seen that hyperthyroid patients tolerated the drug extremely well, and that they were particularly benefited by effective pre- and post-operative narcosis. It soon became evident that the surgical treatment of Graves' disease had changed from being a dangerous and harassing adventure to a reasonably safe calm routine affair. It is in this field that avertin has been of greatest service. Many papers and notes were published in the Journals on this, and I refer to two of them only. Among the first of these was an early account in the *British Journal of Anæsthesia* for October 1930 of Ivor Lewis's observations on 20 cases either of Graves' disease or of toxic adenoma, in which anæsthesia was preceded by avertin narcosis. The series was small, but the cases were carefully observed and the results were an encouragement to further trial, and a sample of what was to come. The second paper covers a series of 243 operations on 220 patients, and was published by Mr. Geoffrey Keynes in the *British Medical Journal*, 1934 (i), 844. In recording an immediate operative mortality of only 1%, the author remarks that the general operative risk of most of his cases was considerable, and that he "cannot avoid the conclusion that this low mortality is to be attributed to some extent to the systematic use of rectal avertin".

On September 9, 1933, H. K. Ashworth of Manchester startled us by an article in the *British Medical Journal* showing that our confidence in Congo-red was misplaced. He showed that solutions which were apparently neutral on testing with Congo-red appeared as acid when tested by "Universal Indicator". In actual fact, many of us jibbed at this new idea and might, perhaps, be described as "Congo-red reactionaries". It has since been stated that Universal Indicator is too sensitive and that it will condemn many a

good solution. Be this as it may, I must say that Ashworth should be considered as being in the right; better that a sea of innocent solution be wrongly poured down the drain than that one dose of decomposed avertin be given.

Since tribromethyl alcohol had proved a satisfactory narcotic, why should not trichlorethyl alcohol be equally as good? Molitor and Robinson in 1938 published in America an account of the effects observed when this drug was given orally to mice and rats, and rectally to dogs and rabbits. They found it to be slightly more hypnotic than bromethol, but to cause less respiratory depression. It was not seen to cause any damage to any of the animal tissues, and there would seem to be no objection to its being used in humans. In this country it was tried by Langton Hewer of St. Bartholomew's Hospital and Douglas Belfrage of St. George's. This was again at the instance of the Anæsthetics Committee, and the findings were published in the *British Medical Journal* of December 3, 1938. As this new drug was a stable liquid, and was easily soluble in water, it was disappointing to find that in some cases it caused excitement both during the onset of narcosis and during recovery. This was exactly what bromethol avoided. In all cases there was with the chlorine compound a tendency to tachycardia, more marked in those who were excited. Finally, Case 18 died suddenly from cardiac failure early in the onset of narcosis. The patient, it was true, was an auricular fibrillant, but the suspicion that the trichlorethanol might have produced the untoward result was enough to put an end to further experimentation. D. A. Wood, in the United States, also recorded a death, this of an apparently robust man of 24 who was being encephalographed under chloroethanol. Cardiac failure was preceded by extrasystoles. This case was the American twenty-fifth—and the last. *Sic transit chlorethol!*

It naturally occurred to a number of workers to try avertinization by the intravenous route. Haffner and Kirschner are reported to have injected small quantities for induction in Germany in 1929-30. In 1941 I saw the method used for anæsthesia in Professor Macintosh's Clinic at the Radcliffe Infirmary, and I am told that it was used abroad in the Army, but I have no details of this last.

Two main aspects of the value of avertin still remain for our general survey—its use in cases with chest troubles, and its use for operations in the mouth and throat.

Being absorbed through the colonic mucosa, and being excreted by the kidneys, avertin was at once welcomed as likely to be particularly useful in cases of respiratory disease. The realization that considerable operations could be easily carried out under avertin narcosis, with superadded gas-oxygen only, seemed to give the answer to many of the problems facing us. The introduction of cyclopropane, however, altered the picture quite fundamentally, and the comparative advance of avertinization was a mere faltering before the rapid strides which followed.

It began to be obvious that prolonged basal narcosis was in itself a contributory factor to post-operative chest troubles. This general idea was developed in some detail by Massey Dawkins who, in 1936, published an extensive series of figures from which he demonstrated that the introduction of basal narcosis had been followed by a doubling of the incidence of pulmonary complications. Avertin, then, was not the best answer to surgery in the presence of chest lesions; in fact, it could even be shown to be the wrong answer.

In throat surgery things took an exactly opposite course. Avertin, it was found, affected the cough reflex to an unusually small extent. By 1933 Shipway was able to recount 244 successful tonsillectomies using avertin as a basal narcotic, and it is now the general experience that, with standard dosage and with due discretion in the administration of the supplemental anæsthetic, there is no contra-indication to the use of the drug in these cases.

Indications for the use of avertin as they now appear to me are easily enumerated:—

- (a) Hyperthyroidism, thyrotoxicosis.
- (b) The expressed wish of the patient.
- (c) The absence of easily seen superficial veins, which renders intravenous pre-medication difficult or even impossible.

Contra-indications are more numerous and cover a much wider range. They comprise:

- (a) Inflammations or lesions of the rectum or lower bowel.
- (b) Operations in the region of the rectum, where a dry field is cleaner than one awash with unabsorbed water of our injection.
- (c) Any condition of the patient which produces a definite deviation from the physiological norm—fever, wasting, anæmia, obesity, cardiac or respiratory lesions, hypopæsis, hyperpæsis, gross renal or hepatic lesions and, though it is rarely met with, myxœdema.
- (d) Mental deficiency (of the chin, not the mind). Holding up an absent chin is a task beyond the powers of the ordinary ward staff.
- (e) Shortage of trained ward staff.
- (f) Inability from lack of time or other reason to clear the patient's lower bowel. If in such a case it is still considered advisable to use a rectal anæsthetic, evipan can be substituted; the necessary solution is very small in quantity, and is much less likely to be returned.

This refusal of avertin to all cases which are in any way ill or physiologically abnormal, implies a personal reconnaissance on the part of the anaesthetist. It is to be hoped that this is now a matter of normal routine.

Having decided on avertin, all that we need ask in the way of special preparation is a simple enema given somewhere between twelve and six hours before the operation. Should the patient ask for a sleeping draught the night before, it is as well to reassure and dissuade him. If he insists, the minimal amount must be given and it must be taken at least twelve hours before the intended time of the avertin. One of the few cases I have had where resuscitative measures have been required for depression solely due to the avertin was in a woman who was allowed to take her usual two allonal tablets the night before. What we did not know till later was that her practitioner had also given her permission to take a further two at 2 a.m., if she then found herself awake. This she had quietly done, and although she did not seem unduly sleepy when the nurse went to give the avertin, yet half an hour later she had to be revived.

The dosage of avertin and the giving of adjuvant drugs present entirely different problems according to whether the patient is normal or is thyrotoxic. With normal patients we can use a standard dosage of one-tenth of a gramme of avertin to each kilogram of body-weight, subject to a maximum of 8 grammes. This maximum corresponds to a body-weight of $12\frac{1}{2}$ stones; although we have avoided the purely obese patients, yet it appears in practice that heavy doses are to be avoided even in heavy patients. By happy chance this limit of 8 grammes coincides exactly with the 8 drachms maximum for rectal paraldehyde. Even more incidentally, the rate of one-tenth of a gramme per kilo is very nearly equal to two-thirds of a gramme per stone. This gives a quick rough check on the amount ordered, though it would be barbarous to mix one's categories by ordering in such a manner. With the standard dosage I also order a hypodermic injection of one-hundredth of a grain of atropine to be given ten minutes after giving the avertin, which takes place between forty and thirty-five minutes before the scheduled time of operation.

Although we hear so often that ether is a drug of the dead past, yet it continues to be used in quite large quantities, and I feel that the giving of a small amount of controllable ether to a normal patient is better than reinforcing the avertin with morphia, than increasing the dose of avertin, or than cutting down the oxygen percentage in the gaseous mixture.

Using this standard dose in a standard patient I expect to find and do find pin-point pupils which dilate on my pinching the skin of the forearm. At the same time there is usually a delayed and vague gesture of the arm, and possibly a turning of the head. Were I to try for them, I have no doubt that I should find the conjunctival reflex absent and the corneal reflex very slight.

In dealing with the thyrotoxic patient, the routine we have just considered is of little value; each case has to be treated on its own merits or demerits, and even during the course of the operation, plans may have to be reconsidered. Furthermore, the surgeon's habits as regards local infiltration, and his views on the advisability or otherwise of intubation, have to be taken into account. It would seem that avertin would provide an excellent means of "stealing the thyroid", but I have had a disappointingly large number of failures, largely, I believe, because my cases have been treated in general hospital wards where it seems almost inevitable that some injudicious remark by nurse, charwoman or neighbouring patient gives the game away.

I like my thyroid case to have a hypodermic injection of either morphia one-sixth grain with atropine one-hundredth grain, or of omnopon one-third grain with scopolamine one-hundred and fiftieth grain, preferably the latter, one hour before the operation. Half an hour later I give, or am present at, a rectal injection of avertin at our standard rate. I keep more avertin in reserve and give anything up to a further quarter dose before the actual operation, occasionally before the patient is moved to the theatre. Then, if the operation is difficult or long, I am ready to give a further quarter dose after the lapse of another half an hour.

To summarize this: first the omnopon-scopolamine; in half an hour, a standard dose of avertin; in another half an hour, an additional dose up to one-quarter of the original, if need be; then the operation, with anything up to a further quarter dose at the end of another half an hour, if necessary. This is not a rigid routine, merely the maximum I consider permissible.

Finally, I should like to express my own personal gratitude to one of the authors of that first paper, Dr. Joseph Blomfield, and to record the appreciation due to Messrs. Bayer, the original manufacturers, for the way in which they held up the sale of the drug until the Anaesthetics Committee had reported upon it.

Section of Comparative Medicine

President—W. A. POOL, M.R.C.V.S.

[October 10, 1945]

The Eradication of Tuberculosis in Cattle. Disease in Relation To Animal Husbandry

By W. A. POOL, M.R.C.V.S.

DURING the last century there have been enormous developments in the characters of livestock. With improved capacity to grow and store foodstuffs, together with changes in the nature of the fodder grown, there has been a revolution in animal husbandry. Improved breeds with characters particularly valuable to the community have been evolved. Stocking has become heavier, animals which mature much more quickly than their ancestors have developed and their production has reached standards which are out of all proportion to what might be regarded as natural for living creatures. Animals have become machines with a standard of efficiency that even engineers might envy. In selecting animals for breeding the aim has been to produce particular characters, for example, special capacity for production, such as milk yield or carcass type; at the same time stamina and disease resistance have been neglected. Consequently, the environment and systems of husbandry have tended to produce a high disease hazard, which the animal has a limited capacity to withstand unless it is given the extensive protection of such measures as are available from veterinary science.

Infective disease of the chronic insidious endemic type, such as tuberculosis, has proved to be much more difficult to control than the acute plagues, even after its nature was understood.

The wastage from disease in this country is a source of great anxiety to all concerned and this has been evinced publicly by many representative bodies with a knowledge of the position—by the farmers themselves, the National Veterinary Medical Association, Government departments and, in a recent memorable debate, the House of Lords.

The extent of tuberculosis in cattle in Great Britain.—There is a lack of adequate data concerning the incidence of tuberculosis in cattle in this country. The Cattle Diseases Committee of the Economic Advisory Council reported in 1934 that about 40% of the total dairy stock in Great Britain might be considered to be infected. The National Veterinary Medical Association in a recent report accepted an incidence of 40% as a reasonable working figure, stating that local incidence varies from 5% to 90% and that 0.5% of cows yield infected milk. A figure of 7% to 10% is commonly accepted as the incidence of tubercle bacilli in churn milk and it is considered that practically all samples from large bulked milk containers are infected.

Infection in cattle due to tubercle bacilli of types other than bovine.—Infection of pigs with the avian type of tubercle bacillus is common and this type can be passed to cattle from either infected poultry or pigs. The lesions in cattle are of a very restricted nature and do not cause clinical evidence of disease.

The human type of tubercle bacillus can cause a very mild infection in cattle, in this case also without resulting in clinical evidence of disease. Such infection of cattle is considered important in Scandinavian countries.

The significance of infection in cattle with acid-fast bacteria other than the bovine type lies in the fact that the animals become sensitized to tuberculin; this results in an added complication in control measures based upon the removal of reactors to that test. There is another probable cause of sensitization, hitherto of a rather mysterious nature; it is a condition in which there are skin lesions associated with abundant acid-fast bacteria. The organisms have not been cultivated and all attempts to set up infection with them have failed.

Tuberculosis in human beings due to infection from cattle.—G. S. Wilson (1942) and Roodhouse Gloyne (1944) have discussed in considerable detail the extent to which human beings acquire infection from cattle. In non-pulmonary tuberculosis the bovine type of bacillus has been found to be the cause in about half the cases of cervical

gland infection and lupus, one-third of the cases of scrofuloderma and one-quarter of the cases of meningeal, bone and joint, and genito-urinary infection.

When the type of bacillus responsible for pulmonary tuberculosis in human beings was ascertained the bovine type was found to be responsible in from 1% to 8% of cases.

Other infective diseases transmitted by milk to human beings.—G. S. Wilson (1942) emphasized that our knowledge of milk-borne diseases is very incomplete, and that the number of recorded cases of disease represents a gross underestimate of the real incidence. He considered that 400 to 500 cases of *Brucella abortus* infection occur annually in England and Wales, the great majority of these being milk-borne. It may be noted that a herd in Staffordshire was found in 1940 to be infected with *Brucella melitensis* and that two other herds had been found to be similarly infected. It is not expected, however, that this organism will gain a foothold in this country.

Scarlet fever and septic sore throat are not infrequently spread by milk, and epidemics are reported from many countries. The causal organism, *Streptococcus pyogenes*, can cause mastitis in the cow and it appears that an infected attendant can pass the organism to the cow's udder.

Alternatively, the milk can be infected directly by a milk handler. As the organism cannot develop in milk under normal trade conditions, direct infection by a milk handler only causes small outbreaks or sporadic cases, but milk from an infected udder can cause serious epidemics.

The organisms of diphtheria, enteric fever, dysentery and cholera can gain access to milk from infected sources. Milk is believed to play an important part in the causation of summer diarrhoea in infants.

Bact. typhi-murium, *Bact. enteritidis* and *Bact. enteritidis* var. *dublin* cause infection in cattle and in such circumstances the milk may be infected and give rise to epidemics in human beings. Staphylococcal mastitis of the cow leads to the development of the powerful and relatively heat-resistant toxin in the milk, with serious effects on those who consume it. The Government "White Paper" (1943) on Measures to Improve the Quality of the Nation's Milk Supply is an important landmark in the campaign to prevent milk-borne disease.

Farming and Political Economy

The prosperity of farming is dependent upon political matters over which the industry has no control. It has been impossible for farmers to foresee what conditions would prevail for any considerable period in the future. There have been periods of unnatural prosperity, with rocketing prices in time of war, and periods of serious depression between the wars. Political considerations have decided both the competition which has to be met in the sales of the farmers' products on account of importation from countries outside the British Isles, and also the conditions under which many of his essential supplies are imported.

In such circumstances, there has been little opportunity for the individual to depart from accepted practice and the conditions have not favoured the introduction of desirable changes to prevent disease.

The Marketing of Cattle

Systems of marketing cattle in the United Kingdom appear to have evolved which, while providing a certain convenience to the vendor and purchaser, do not give sufficient opportunity for the latter to be reasonably certain that he will obtain a healthy animal. This is rather strange because good health is the first character the buyer expects in his purchase. The buyer relies upon his judgment which is based chiefly on cursory observation of certain external characters: this is of course useless for the detection of disease, except in the case of certain of the more obvious conditions.

Self-contained and "Flying" Herds

For disease control the self-contained herd is in the strongest position. At the other extreme, the "flying herd" is obviously a bad risk with regard to disease. The modern development of the milk industry has led to the adoption of the "flying herd" system on a very large scale. Commercial dairy herds have to maintain a steady output of milk and so cows in milk yield have to be maintained. New purchases have to be made at relatively short notice to replace cows which cease to yield milk. The system of marketing does not provide a good supply of really healthy calving cows of suitable types. Purchases tend to be made blindly; disease is introduced, or perpetuated, and this makes further purchases necessary. In this way the industry is producing its own problems instead of solving them.

It is known that "flying herds" have a high rate of tuberculosis and that they are the most difficult herds to deal with when eradicating the disease.

The Design of Farm Accommodation

Farm buildings are often old and difficult to improve and this requires attention.

Savage (1929) in his book, "The Prevention of Human Tuberculosis of Bovine Origin", was very critical of the hygiene of cowsheds. He said: "Many of the existing cowsheds seem to be constructed and used as if their object was to spread infection as easily as possible." Another quotation from his book is worth recording: "The elaborate evidence as to droplet and cross-infection in dormitories might as well have never been acquired for all the influence it has so far exerted upon cowshed construction." Although this was written sixteen years ago it would be difficult to suggest that it does not apply to farms to-day. Observations made in hospitals during the war on the spread of infection by bedclothes and floor dust have considerable bearing on conditions in houses used for animals.

When planning farm buildings insufficient attention has usually been given to isolation arrangements.

The fact that animals feed off the ground, on which they defæcate and micturate, is of course a key problem which has to be studied in the development of successful animal husbandry. The great advantages which accrue to husbandry from these very habits have been fully utilized; they are natural habits and become problems only when domestication requires a concentration of animals. The problem is the old one of "overcrowding".

Water Supply on Farms

The provision of a suitable supply of pure water is commonly a great difficulty both inside buildings and at pasture. Deficiency in the supply of water available on farms causes serious breakdown of essential hygienic standards. Cleansing is impossible and disease factors are given undue opportunities to operate. A Government "White Paper" on water supplies was issued in 1943 and if the plans there described become operative a great advance will have been made, but it is doubtful if farms will get all the service that is required.

Drainage in farm buildings.—Like water supply, the provision of adequate drainage for farm buildings is important and is often insufficient.

The Pasteurization of Milk

Little need be said beyond assuming that at last there is no serious opposition to its adoption for all milk except that produced hygienically from herds free at least from tuberculosis, brucellosis, mastitis and any other contagious disease, provided that the pasteurization is properly achieved.

It is understood that a pasteurization policy involves adequate measures for the provision of milk from animals that are not infected with the preventable diseases, so a pasteurization policy should not be allowed to hinder the abolition of disease from our herds.

THE CONTROL OF TUBERCULOSIS IN CATTLE

The control of tuberculosis by immunization.—The extent to which large-scale immunization can be used as a serviceable measure for the control of tuberculosis is still unknown. BCG vaccine appears to be at least of some value in suitable conditions for preventing serious clinical manifestations of infection. If further tests of this or any other method of immunization yield evidence that a really useful immunity can be conferred on cattle, such a vaccine could be employed in certain circumstances as part of a control campaign.

The chemotherapy of tuberculosis in cattle.—At a time when specific chemotherapy of bacterial infection is under such intensive study and yielding such spectacular results, it might be suggested that there is justification for delay in commencing eradication by other means, in the hope that some important discovery will revolutionize the position with regard to tuberculosis in cattle. Whatever might be the chance of finding a successful curative agent, it is certain that proof of its efficiency could be provided only after extensive trial, first on laboratory animals and later on cattle. Its cost would have to be low and its administration economical, if it were to be of value for the control of such a widespread disease. Whatever the future may hold in this respect, control by the elimination of infection, using the powers now available to science, should be the aim at the present time.

Meat inspection in relation to the control of tuberculosis in cattle.—In the application of any control plan it would be necessary that important sources of information con-

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enhanced price for milk from herds that are free from the disease. Unless there was a considerable difference between the value of the sales from such herds and those still infected there would not be sufficient inducement for the farmer to co-operate willingly. Furthermore to grant such a subsidy would be the fair way to spread the cost of an eradication campaign over the community which would benefit from it.

In the earlier stages of an eradication policy an "Areas Plan" must be used. This is probably universally accepted. In the areas first chosen there should be a good proportion of herds free from the disease, or only lightly affected. The types of cattle-farming practised would influence the choice of areas and the localities selected should have natural boundaries. In such areas all cattle would require to come under control. As the disease was eliminated the areas would be enlarged until ultimately adjacent areas would join, thus making an extensive "clean" area. New areas would gradually be declared until they all joined.

At the same time it would be advantageous if voluntary eradication were undertaken, with full help from the Government, including financial assistance, in parts of the country outside the declared areas. This would tend to increase the supply of "clean" animals for herds under eradication, besides enlarging the number of centres from which the best form of propaganda, actual example, would issue. In this way, too, fresh localities would automatically become ripe for declaration as new *areas*.

For the eradication of tuberculosis from cattle it is axiomatic that the animals should be shielded from infection from other species of animals including birds.

Animals in a latent stage of tuberculosis can of course often be used with a good deal of success. Indeed, if the fact that the infection was present were known and suitable precautions were taken, there would not be a great deal of objection to utilizing a good many animals in this category in certain types of herds until they could be disposed of economically and with safety to the community, provided that adequate precautions were taken to render their products harmless to human beings. Thus reactors free from clinical signs of infection could be moved from herds in the declared area to herds elsewhere and be utilized in this manner, so long as the herd in which they were placed was known to have a large proportion of reactors.

The case for eradicating tuberculosis in cattle rests chiefly upon economic considerations. The disease is responsible for great wastage. It considerably shortens the productive life of the animal, diminishes the return obtained for the food consumed, the replacements needed on account of tuberculosis cause additional expense, and labour is wasted. Tuberculous animal food products have to be condemned as unfit for consumption.

Apart from finance, the difficulty in undertaking eradication in this country arises from two main factors, a shortage of healthy cattle to replace infected animals and a shortage of veterinary surgeons to undertake the work.

There is no short cut for the supply of healthy animals to replace those to be eliminated under an eradication scheme, though much could be done to improve the position in the future. When an efficient eradication policy has been in operation for a certain time, a stage will be reached when so many herds are free from infection that a supply of tuberculosis-free cattle will be available. It is possible that a large number of tuberculosis-free animals could be obtained from the other side of the Atlantic.

The shortage of veterinary surgeons is to be regretted and it is to be hoped that plans at present under discussion will provide them before long. There has perhaps been some undue caution in the calculations of the number of veterinary surgeons required in the future. Tuberculosis is only one of the diseases to be eradicated from our livestock. *Brucella* infection will probably have to be similarly dealt with one day. Future research may be expected to provide means for dealing effectively with certain other diseases which are intractable at present, and there again, for a time, additional veterinary staff will be required. It would be quite safe to make provision for a period of expansion of not less than fifty years, and in these circumstances there need be little hesitation about launching adequate educational schemes for to-day.

ENQUIRY INTO MEANS FOR THE CONTROL OF TUBERCULOSIS IN CATTLE

While much has been said about what could be done, there has not been sufficient general investigation of the situation as a whole. Action to overcome one part of a general problem may increase difficulties in other respects.

Tuberculosis is an example of a disease, for which a far greater and more concerted effort is required than has hitherto been envisaged. The problem involves finance, medical and veterinary science, engineering, public services such as power and water,

cerning the extent and incidence of the disease should be studied. The carcasses of cattle slaughtered for any purpose provide a master-key to the study of the question. It would therefore be specially valuable if there were close collaboration between the departments responsible for meat inspection and for knackeries and other means of disposal of diseased animals. Where necessary the disease could then easily be traced back to the farms of origin, and so provide an invaluable check on the efficiency of the control measures.

It may be added that in the eradication campaign so successfully carried out in the United States of America the Federal Department of Agriculture had this source of information at its command.

Disinfection.—In a tuberculosis eradication campaign disinfection is a most important item. To obtain the best results the use of suitably equipped teams is valuable. In the United States special lorries provided with a petrol-driven pump are used. After the routine cleansing and removal of litter the disinfecting team deals systematically with the building, using a suitable disinfectant applied hot and sprayed under pressure.

Instruction of farmers and their employees on matters concerning disease control.—Those responsible for the care of livestock, including the owner, the man in charge of the herd and the cowman, must understand the conditions which lead to infection and those which control it; how the germ of the disease operates in the body of its host and outside it, and the extent to which an apparently healthy animal can itself develop severe disease, or infect another animal.

In herd management there must be continuity in any system that is practised and this involves the need to ensure that there is no alteration of special routine when one attendant replaces another, such as when duties are changed around while members of the staff are off duty or on holiday. This is often, of course, a matter of extreme difficulty and there is, therefore, all the more need for an inflexible system in order to avoid breakdown.

In spite of the amount of semi-scientific literature that is produced there is a dearth of suitable books and booklets for the layman explaining the manner in which disease can spread and how those responsible for the animals should do their work in order to eliminate this risk. Something roughly comparable to the course of instruction in the first-aid books of the Red Cross and St. John Ambulance Societies is needed, except that it would not deal with first-aid. It should be devised specially for persons with an elementary school education and deal with the hygiene of the farm.

To be effective such instruction should be given so that it is really convincing and is understood; it should therefore be arranged in a manner which is suitable for the mentality of those concerned. There is probably a case for teaching some of the matters concerning disease control in rural schools. Suitable leaflets, handbills and slogans used discriminately would be most useful. Lectures should be given on a wide scale. Suitable instructional films would be of particular value, with arrangements for their exhibition at small gatherings, so that they might be seen repeatedly by most of those concerned.

Complete eradication.—In the United States of America spectacular success has been achieved in a nation-wide eradication campaign and within a quarter of a century the incidence of reactors has been reduced to less than 0.5% in every one of the 48 States. In Canada great success has also been achieved.

In Norway the disease hardly exists in cattle and there was little in Finland when war broke out. Other Scandinavian countries have large numbers of herds free from the disease. In most other countries where tuberculosis is a serious problem the results of control measures have been poor or mediocre, but in some there are large numbers of herds free from the disease as a result of such measures, though with few exceptions the herds are scattered.

In many European countries there has been a serious overestimate for many years of the extent to which tuberculosis can be controlled by the detection by clinical methods of cases of the "open" type and the elimination of such animals from the herds. During the decade prior to the recent war there was a striking change in many countries towards reliance primarily on the tuberculin test. As soon as it was made worth while in various countries for the farmer to rid his herd of the disease, under schemes providing financial assistance to replace reactors and an increase in the price paid for milk from clean herds, good results began to be reported.

It is now quite clear that nothing short of the regular application of the tuberculin test and the elimination of reactors, together with regular veterinary inspection to detect clinically affected animals, will achieve success, and that considerable financial assistance must be given for the replacement of animals that are condemned, together with an

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Some Chapters in Cambridge Medical History V. Clifford Allbutt and the Transition from the Nineteenth Century¹

By SIR WALTER LANGDON-BROWN, M.D.

FORMERLY a speech was delivered annually in the chapel of Caius College, Cambridge, on the progress of medicine from the time of Dr. Caius. On May 11, 1870, it fell to the lot of Thomas Clifford Allbutt to deliver this. In scholarly and eloquent terms he showed that theories of disease were undergoing a great change; disease was not something with an independent existence, but is "the living body in a peculiar state", and the function of the physician was "to put the body in such a position that it may most quickly recover its own balance". He believed that chemical inquiry was already finding the way into many of the remoter secrets of function and looked forward to the construction of some sort of canon for the discovery and adaptation of remedies, "an achievement" as he said "which would at once raise Medicine into the front rank of intellectual pursuits". Far though we may still be from realizing that canon, his other contentions, so apart from the thought of 1870, are now part of our common inheritance and justify him in speaking of him as the exemplar of the transition from 19th to 20th century medicine.

It is impossible here to give a detailed account of all he accomplished in nearly ninety years of life, nor is it necessary since it has been done so admirably by Sir Humphry Rolleston in a book to which I am much indebted for many of the facts I shall relate. In the main I shall concentrate on three things, the forward direction of his thought, his work for the Cambridge School as Regius Professor of Physic, and his remarkable personality as I remember it. Some biographical details are, however, essential.

Thomas Clifford Allbutt was born at Dewsbury, Yorkshire, on July 20, 1836, the only son of the Reverend Thomas Allbutt. His mother was a Wooler, a family closely associated in friendship with the Brontës. Allbutt's impression was that Emily Brontë was a most unagreeable woman, with whom no one could get on except Charlotte, whom he thought "as dull as a governess ought to be". Five of his uncles were medical and he had a free run of the surgeries of two of them and he was fascinated by the strange labels, "mummy powder", "horn of unicorn" and "crabs' eyes". He was also a diligent student of the *Lancet* when only 9 or 10 years old. He had a small laboratory at home where he was always making experiments. His delicacy as a child he afterwards attributed to the "sparkling water" of the Vicarage well that gave him a continued fever, treated by avuncular bleedings, antimony, mercury, and blisters which left lifelong scars on his back. Thus from the very beginning he was interested in the past, suffered from the present and looked forward to the future of therapeutics. He went to the famous and ancient St. Peter's School, York, of which the great Alcuin, who stimulated Charlemagne to found the Cathedral schools, had been Master from 772-782.

His father had been at St. Catherine's College, Cambridge, but he entered Caius in 1855, where he obtained a classical scholarship; however, he soon determined to read natural science. Among his contemporaries there were four men all destined to become well known in medicine, Howship Dickinson, W. B. Cheadle, George Hare Phillipson and Peter Wallwark Latham, with the last-named of whom he later came into conflict, while the first-named was a lifelong friend. He graduated alone in the first class of the Natural Sciences Tripos, which had been established only eight years previously, although music, art and literature had attracted him at Cambridge more than science. Nevertheless he attended the teaching of George Paget and George Humphry at Addenbrooke's before going to St. George's Hospital whither Dickinson also went. He was clinical clerk to Bence Jones of whose brilliant and whimsical personality he has left an entertaining account. J. W. Ogle also had a considerable influence on him, directing his attention to the ophthalmoscope. He also worked with Lockhart Clark. Bence Jones advised him to study in Paris where he attended the clinics of Trousseau, Charcot, Duchenne and Bazin, and became very friendly with Raynaud. Thus he received a thorough grounding in mid-nineteenth century medicine.

Returning to England in 1861 he decided that, with his Yorkshire associations, Leeds was the place for him to settle in, and there he remained for twenty-eight years. Almost at once he was elected physician to the Fever Hospital, where he introduced fresh air, as an important factor in the treatment of typhus, and methods of prevention of post-typhoid thrombosis. His experience there enabled him in Cambridge, in 1903, to recognize an outbreak of alastrim for what it was, though doubters dubbed it "All-but smallpox". In 1864 he became physician to the Leeds General Infirmary, which

¹ Chapter I, "John Caius and the Revival of Learning" (1942), *Proc. R. Soc. Med.*, 35, 61.Chapter II, "Francis Glisson and the Insurgent Century" (1943), *Proc. R. Soc. Med.*, 36, 17.Chapter III, "William Heberden and the Age of Reason" (1944), *Proc. R. Soc. Med.*, 37, 53.Chapter IV, "The Early Nineteenth Century from Pennington to Paget" (1944), *Proc. R. Soc. Med.*, 36, 663.

trade—both national and international—systems of husbandry, economics, industry and man-power.

There is a need for a detailed integrated report, representing all the interests concerned, on the requirements for the eradication of the disease.

Tuberculosis stands out as the major preventable animal disease in this country. Other diseases which now ravage our animals also require energetic attack at the earliest possible moment. One of the greatest contributions of a tuberculosis eradication scheme would be the stimulus and actual aid it would provide for the control of certain other diseases.

CONCLUSIONS

In this country, in spite of all that has been done, the quite extensive legislation of the last thirty years, the pioneer work done by the veterinary officers of the Ministry of Agriculture and Local Government Authorities, by the other scientists and by agriculturists, the present position with regard to tuberculosis control might be described as "the end of the beginning". Even so a very great deal has been accomplished. The scientific work to provide the essential knowledge has been done. A great wall of opposition has been broken down. The leaders of agricultural interests are clamouring for action. The veterinary service is organized, but at the present time it is numerically insufficient to undertake even the next stage which the Government is anxious to put into effect. Many more veterinary graduates are urgently required.

All milk except that from herds free from tuberculosis and the other important infective diseases should be pasteurized, and there appears to be little objection to the pasteurization of all milk.

An intensive educational programme, covering the requirements of both the workers in the cattle industry and the consumers of their products, should be undertaken. A suitable manual is required for the instruction of animal attendants.

Much could probably be done within the cattle industry to assist this control work. The marketing of cattle is not well organized with regard to the opportunity for the purchaser to select healthy animals. In existing circumstances it is difficult to control disease in the "Flying Herd".

Agriculture requires a long period of steady prosperity. Farm accommodation is often inadequate. Water supplies must be improved.

An "area" system for the eradication of tuberculosis should be started as soon as possible.

An inquiry into means of controlling tuberculosis and a detailed report embodying all the interests concerned in the problem are required.

The methods used in the eradication of tuberculosis will have a great influence in due course on action to be taken for the control of other infective diseases of farm animals.

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being "Joseph Vance" and "Alice-for-Short". It happens that I know something of those years, for that wonderful old lady, Mrs. Russell Barrington, whom I knew well, lived next door to the Allbutts and was their close friend, often travelling abroad with them. It was the very heyday of Victorian prosperity, when Royal Academicians counted for something. It has often been alleged that George Eliot drew the portrait of Lydgate's Middlemarch from Clifford Allbutt in 1872, though obviously the portrait of Lydgate's wife is in sharp opposition to the real Mrs. Allbutt as she then was. George Eliot knew them well, but G. H. Lewes told Sir James Paget that she had never known a surgeon intimately. There is an obvious quibble here, for the novelist could easily turn a physician into a surgeon, and Allbutt himself was always a little self-conscious when taxed with the story. At any rate there is no doubt that he was the hero of Mrs. Russell Barrington's novel, *A St. Luke of the 19th Century*, for she told me so herself. She was the sister-in-law of Walter Bagehot, the well-known economist and writer, and knew all the literary and artistic celebrities of her day, which was a long one since she lived to well over 90. A dominant interesting personality, she acquired the nickname of the Duchess of Kensington, and held a circle in a house that was a museum, with a music room frescoed by Watts. In this pleasant setting Allbutt was very happy and when in 1892 the offer came of the Regius Chair at Cambridge it is not surprising that he hesitated before accepting new responsibilities. Little could he have realized that the greatest part of his career was yet to come and would occupy one-third of a century.

Sir George Paget, who had held the Chair with conspicuous success for twenty years, had died on January 29, 1892, at the age of 82. It had been usual for a resident to be appointed and now that more than half a century has elapsed there can be no harm done by saying that there were three physicians in residence, any one of whom would probably have been willing, to say the least, to take office. But to have appointed one of them would have roused fierce antagonism with the other two, while to have appointed any of them would have been distasteful to considerable, if different, sections of the University. So it is not surprising that it was hoped that the choice would fall elsewhere. Now of the six Regius Chairs the Crown had retained the right to appoint for three, Civil Law, Physic and Modern History, leaving Divinity, Greek and Hebrew to ordinary Boards of Electors. Sir Humphry Rolleston's statement that Dr. Alex. Hill, Master of Downing, was commissioned to sound Sir Andrew Clark as to his willingness to come, requires some expansion. True, a self-appointed junta meets and makes a recommendation to the Vice-Chancellor who conveys it via the Chancellor to the Crown advisers, but it by no means follows that this recommendation is acted upon. Ultimately the Prime Minister asks the individual selected if he is willing to have his name submitted to the Sovereign. So that it does not necessarily follow that Hill's invitation would have become operative, though Sir Andrew's eminence makes this highly probable. Anyhow he declined, as did Allbutt, whose name apparently had been suggested by Sir Michael Foster. Fortunately, Sir William Broadbent, on behalf of Her Majesty's advisers, succeeded in persuading him to accept. Here again Foster proved himself a supreme judge of man. It was the psychological moment for such an appointment. The medical school had achieved great internal success, and now there was a man who could make it equally successful externally, carrying its influence outside Cambridge to the world at large, for there was nothing parochial about his outlook.

Well do I remember his inaugural lecture given in May 1892. His handsome, dignified, well-groomed appearance made an instant appeal. Still more impressive was the substance of a lecture blending science with the humanities which gave me a new outlook. It was really a decisive influence in my life. Little did I dream then that forty years later it would fall to my lot to give the lecture on a similar occasion, though not, I fear, with such impressiveness. It is not easy to wear the giant's robe.

The coming in of a Regius Professor from outside Cambridge led to an unfortunate complication, for previous occupants of the Chair had been physicians to Addenbrooke's Hospital prior to appointment. I referred in my last paper to the Downing Chair of Medicine which was occupied at the time of Allbutt's appointment by Peter Wallwork Latham. He was specially learned in organic chemistry, making original observations and advancing interesting views. He had a large practice and was much beloved by his patients. Yet when it came to University matters his genial appearance proved to be entirely misleading, for he was a good harer and a bitter controversialist. The quarrel over his emoluments dragged on for some years. His contribution to the medical school may be summarized as throwing a spanner into the works whenever occasion offered!

A characteristic action of his followed Michael Foster's resignation from the Chair of Physiology in 1903. Since for more than thirty years Foster had laboured incessantly and most successfully to build up the modern Medical School at Cambridge, a proposal was made by Allbutt and others that an extraordinary salaried Professorship should be created for him as a kind of pension. Latham violently opposed this and actually issued a fly-sheet belittling Foster's services to the University. Consequently the project had to be dropped.

One can accordingly realize that an attempt to obtain rights at Addenbrooke's for

then had on its surgical staff Samuel Hey, Wheelhouse and Pridgin Teale junior; with the last-named he became closely associated. Up till then, Leeds had been more renowned for surgery than medicine, but he speedily rectified that. Lord Moynihan said that Allbutt and Teale were pioneers of team-work. A new building, the first in England on the pavilion principle, was erected in 1869, which greatly facilitated their co-operation. Allbutt held a large number of posts in the Medical School, and gradually acquired a large consulting practice, though he said for some years he was "politely postponed as too young for confidences". So he filled in his waiting time with many papers and reviews. As Sir Humphry Rolleston remarked, "a striking feature of his life's work was the persistent way in which he returned to and expanded any subject on which he wrote; this is well shown by the progressive development and scope of his writings on cardio-vascular and nervous diseases and medical history". In 1867 he introduced the clinical thermometer now in ordinary use. The one with which Wunderlich had made his pioneer observations was a foot long and required twenty-five minutes to register. In the same year his important paper on the significance of skin affections appeared. Then he turned his attention to nervous and mental diseases at the West and East Riding Asylum, the outcome of which appeared in his monograph on the ophthalmoscope, his description of syphilitic disease of the cerebral arteries, six years before Heubner's classical account and his paper on locomotor ataxy. Always an advocate of the use of the hands, he urged the drainage of empyemas and pericardial effusions which he had seen performed in Trousseau's Clinic and gastric lavage as practised by Kussmaul. He also popularized hypodermic medication, which, introduced by Rynd of Dublin in 1844, had attracted very little attention, and he urged, against opposition, the water-borne character of some typhoid epidemics.

In 1869 he married Susan England. They had no children, so they adopted a niece of hers. It was a singularly happy marriage; he told me that when he was away from home he wrote to his wife every day. She was a gracious hostess and shared all his interests; she survived him about twelve years and was well over 90 when she died.

Soon after his marriage, Allbutt was elected a member of the Alpine Club; he had always been an enthusiastic climber from the age of 14 and continued the practice to quite an advanced age. In one of his papers on overstrain of the heart he described how he brought on an attack of acute dilatation of the right ventricle by climbing and how he lay down and percussed out his own enlarged cardiac dullness. Professor Roy (who had a similar experience when, convalescent after typhoid, he had an unexpected call to an accident on the mountains) told me that so far from percussing out his heart, he thought he was going to die and felt no interest in scientific observation.

This was the period in which Allbutt advanced the view that tetanus toxin extended up the peripheral nerves to the central nervous system, but this, although now established, was rejected by a committee of the Pathological Society. His advocacy of cold baths in the treatment of hyperpyrexia was more successful. In 1876 his paper on *Mental Anxiety as a Cause of Granular Kidneys* proved the starting-point of his work on hyperpæsis which he continued for so many years. About this time he became a pioneer of the open-air treatment of tuberculosis—another subject in which he continued to take warm interest for the rest of his life. He also had some severe things to say about "brain forcing" at school, maintaining that precocity was gained at the cost of feeble maturity and early decay and that schoolmasters as a class were utterly unconscious of the existence of the science of physiology. Here then is a whole group of topics where his view was definitely in advance of contemporary thought. As in thought so in conduct, for in 1880, being scandalized by medical expert witnesses contradicting one another in Court, he persuaded those in Leeds to refuse to give evidence except after consultation between both sides, a proceeding highly commended by Mr. Justice Stephen.

As is well known he deplored the divorce between medicine and surgery and induced his colleague Pridgin Teale to introduce the operation for removal of tuberculous glands in the neck. I am old enough to remember the ghastly scars that disfigured so many necks before this advice was generally followed.

In March 1884, having been elected F.R.C.P. in the previous year, Allbutt delivered the Goulstonian Lectures on Visceral Neuroses in which among other things he castigated the prevalent attribution of many ailments in women to small uterine displacements that required continued treatment "except during the long vacation when the gynaecologist is grouse shooting or salmon fishing or leading the fashion in the Upper Engadine". There is no doubt that these lectures had a profound influence on the recognition of the abdominal expression of psychoneuroses. The next month he retired from the active staff at Leeds under the twenty-year rule, but that he was heavily engaged in extensive consulting practice is shown not only by a comparatively small literary output during the next five years but still more by his toying with the idea of retirement at the age of 53. Instead came an interlude of three years in the form of a Commissionership in Lunacy before he was to take up even more important work. Surprise has often been expressed at such an unexpected change, but his asylum work made him suitable for it and it proved acceptable to him. A smaller income was offset by lighter work. He settled at 3, Melbury Road, Kensington, amid an artistic coterie which included G. F. Watts, Lord Leighton, Burne-Jones, Luke Fildes, Marcus Stone and, I think, Frank Dicksee. There was also William de Morgan, brother of the mathematician, who after designing artistic tiles in the Pre-Raphaelite mode, took to writing novels, the best known

pital on the outskirts of Cambridge under the enthusiastic direction of the late Dr. Strangeways. Some years later the hospital beds had to be given up, but the research laboratory continues to do admirable work.

Believing as he did that one of the functions of a University is to teach students to think, he attached great importance to the theses presented for the degree of M.B. and tightened up the procedure. The history of university theses is of some interest. They had replaced the old mediæval "Disputations" in the eighteenth century. That there was abuse of the method is shown in Gunning's reminiscences. He tells of a man named Nicholson in the later part of that century, who used to wander up and down college staircases murmuring "Maps, maps for sale". But this merely cloaked his real mission, which was to act as an agent between candidates and needy dons who provided candidates with theses. His own commissions must have been lucrative for they enabled him to start a bookshop opposite the Senate House, which later was purchased by the Macmillan brothers before they embarked on their London venture. Then the business became Macmillan & Bowes, and is now familiar to us as Bowes & Bowes.

Gradually theses were abolished except for doctorates, for the M.B. and as an alternative procedure for the B.D. Allbutt attached great importance to the style in which the M.B. thesis was presented and was so impressed with the inability of candidates to write decent English that he published *Notes on the Composition of Scientific Papers*, illustrated by choice examples of English as it ought not to be written. As he neatly put it, his quotations were "given for the most part without acknowledgment, for obvious reasons". Indeed, latterly he seemed more concerned about the style than the matter of the thesis. Still his efforts to stem the tide of scientific jargon, masquerading under the title of medical literature, were much needed and were not without effect.

It was complained by graduands that the delay in obtaining their degree caused by the preparation of these theses handicapped them in competing for resident appointments against graduates of other universities, or those qualified by the Conjoint Board. Allbutt met this by securing that the Bachelorship of Surgery, only obtainable when the whole M.B., B.Chir. examination had been passed, should be a registrable qualification. It was also alleged that the whole thing was stultified by literary "ghosts" who wrote the theses. But the cross-examination of the candidates would soon reveal whether the work was substantially his own, some help not being objected to. I only once had reason to be suspicious, and that curiously enough was of an M.D. thesis by a distinguished dermatologist!

It was therefore a great regret to me when my successor induced the University to abolish the M.B. thesis. I regard it as a retrograde step for the following reasons. They gave the young graduand the task of working at a specific problem and presenting his results in due form; these could be discussed with and criticized by a senior man, which should be a help to him when he later embarked on the shoals of "medical literature". It made for good personal relations for every graduand to have a talk of half an hour or so with his Regius. I owed my first personal association with Clifford Allbutt to reading my thesis to him. It induced men to revive contact with their University and College by their having to come up to read their thesis and then take their degree in person, the whole forming a pleasing ritual which distinguishes a University from a mere examining body. Since theses were abolished an increasingly large proportion of men just take the degree by proxy. To the Regius Professor the system had, besides the opportunity of knowing something of each graduate personally, the advantage of finding out just which teachers were influencing the students in the teaching hospitals. I hope I may be pardoned this incursion into controversy, which is dictated by my loyalty to my great predecessor's ideas. His efforts to raise the standard of general education of medical men were unceasing. As he said in 1902: "I have had already to observe to my pain that the Cambridge medical student of to-day is by no means 'learned'; that too often he thinks loosely, and that he does not always write even the English of the gentlemen who do the fires and murders for country journals. On his Latinity I will discreetly keep silence." It may therefore surprise some that he took so leading a part in urging, at length successfully, the abolition of compulsory Greek at Cambridge, but as he said, "If we make Greek optional we can raise our standard of Latin" and he deprecated "the sterile methods of cramming little boys with the abstract propositions of grammatical pedagogues" as a preparation for later passing the Littlego. Allbutt's own distinction as a classical scholar was recognized by his becoming President of the Classical Association and was shown by his great book on *Greek Medicine in Rome*. When this Section was established here in 1912, Osler became President and Allbutt was one of the original Vice-Presidents. It was indeed a fortunate thing for British Medicine that during most of the first quarter of this century the Regius chairs at Oxford and Cambridge were held by men of such outstanding distinction as Osler and Allbutt, so similar in outlook, so complementary in temperament. Those of us who were present at the celebration here of Osler's 70th birthday will never forget the impressive dignity and charm with which Allbutt presented the *Festschrift* to him, nor Osler's beautiful and touching reply, in the course of which he said: "To you, Sir Clifford, in fuller measure than to anyone in our generation has been given a rare privilege; to you when young, the old listened as eagerly as do now, when old, the young." It was indeed that universality of appeal which was Allbutt's great source of influence. In a sense, apart from the handicap of deafness, he never, even physically, seemed to grow old until quite shortly before his death. He could make humorous references to his years such as "that state of mind which seems mellow wisdom to its owner, but appears to the younger generation as senile obstinacy". On another occasion he said that while demonstrating

the Regius Professor met with strong opposition from the same quarter. Latham was credited with saying in the best style of Victorian melodrama that Allbutt would only enter the wards over his dead body. This tragedy was avoided by his resignation from the staff in 1899, and a *modus vivendi* was then quickly established between the University and the Hospital, giving the Regius Professor *ex officio* rights to beds and to teaching in the wards.

Allbutt made good use, however, of his eight years' exclusion from hospital work for he employed them in the production of his *System of Medicine*, a really great literary and scientific work. The introduction is an exposition of his medical philosophy, in which he maintained that there is no more a standard pattern of disease than a standard pattern of man. Disease is not an entity, but a reaction of the whole individual. He disliked the label of "types" though he had to admit their adoption in a *System of Medicine*. This essay was, to the regret of many readers, deleted from the second edition in which Sir Humphry Rölleston collaborated. Possibly the author considered his view, previously regarded as revolutionary, was now accepted and therefore need not be repeated. Fourteen other articles appeared from his pen and I would specially call attention to those on digestive neuroses and on drug addiction as admirable examples of real medical literature.

The last decade of the nineteenth century in which Allbutt took office was indeed an extraordinary one in the history of medical progress. It saw the beginning of endocrine therapy, the first antitoxins, the discovery of X-rays and radium, the start of clinical pathology. To those of us who were students then it seemed, as it had a century before to Wordsworth—

"Bliss was it in that dawn to be alive

But to be young was very heaven."

It wasn't really, but the kindly finger of Time has rubbed out the unpleasant memories and left only the recollection of the thrills and excitement as discovery followed on discovery. Allbutt was always alive to such new developments even to an advanced age. As an instance of this outlook I may quote his remark that during his lifetime medicine had "not so much changed as transformed: a generation ago the doctor was an observer and a naturalist, and by practice mainly an empiric; now medicine was being reconstructed" on a more scientific basis. In the same spirit he kindly wrote the preface for an *Encyclopaedia of Medical Treatment*. I edited in conjunction with the late Keogh Murphy in 1915. After a remarkable résumé of the progress of medicine he said: "On a mountain in Switzerland, far away from books and papers, I have ventured to make this sketch of the new Therapeutics . . . I have rambled at large among the discoveries which have awakened my own enthusiasm . . . What a joy it would be to start from the present and, with these new visions, to begin it all over again!" A striking pronouncement from a man who had just entered his eightieth year. The late Dr. W. E. Dixon, Reader in Pharmacology in the University, bore testimony to this extraordinary freshness of mind when he told me within a year of Allbutt's death that he would still discuss the work going on in the Department and even suggest new experiments.

The breadth and forward direction of his outlook was manifested in many other ways. Thus for years he strongly advocated the study of comparative pathology and was instrumental in founding the Section for this subject in this Society, becoming, appropriately enough, its first President. Always an advocate of fresh-air treatment (though as he put it "not treatment by hurricane") in tuberculosis, he was actively interested in Varrier-Jones' scheme for Village Settlements for tuberculous subjects. At the outbreak of the last war, Varrier-Jones, who was rejected for the Army on account of his heart, that heart which was to fail him so tragically twenty-seven years later, undertook the duties of the Cambridge Tuberculosis Officer, who had joined up. He soon realized that as long as patients were returned to their old environment they were doomed to relapse. So he accordingly ventured to open a small settlement in the neighbouring village of Bourn, with such success that in 1918 he was able to transfer it to much larger quarters at Papworth. Allbutt warmly supported the scheme and became the first President of the Settlement, remaining throughout his life a valued helper and adviser. Much of the success of this plan of rehabilitating patients into suitable industries, while they lived with their families in suitable cottages, was due, as Varrier-Jones declared, to his wise counsel and influential advocacy. In the same way he actively supported Sir Henry Gauvain's work at Alton for surgical tuberculosis.

Then he was always urging the change from the asylum conception to that of the mental hospital, with facilities for investigation and research, the importance of which is now generally admitted. Towards that end he played a large part in establishing the Diploma in Psychological Medicine at Cambridge. It might be thought he was inconsistent in opposing psycho-analysis so vehemently, but it should be remembered this was at a time when its disciples, medical and lay, were indulging in great extremes. It had become a fashion for undergraduates to psycho-analyse one another, often with deplorable results.

Many of the changes he advocated in the medical curriculum are now being brought forward as new ideas forty years later. With the financial aid of his friend Dr. (later Sir) Charles Brown of Preston, he was largely instrumental in establishing a Research Hos-

pital on the outskirts of Cambridge under the enthusiastic direction of the late Dr. Strangeways. Some years later the hospital beds had to be given up, but the research laboratory continues to do admirable work.

Believing as he did that one of the functions of a University is to teach students to think, he attached great importance to the theses presented for the degree of M.B. and tightened up the procedure. The history of university theses is of some interest. They had replaced the old mediæval "Disputations" in the eighteenth century. That there was abuse of the method is shown in Gunning's reminiscences. He tells of a man named Nicholson in the later part of that century, who used to wander up and down college staircases murmuring "Maps, maps for sale". But this merely cloaked his real mission, which was to act as an agent between candidates and needy dons who provided candidates with theses. His own commissions must have been lucrative for they enabled him to start a bookshop opposite the Senate House, which later was purchased by the Macmillan brothers before they embarked on their London venture. Then the business became Macmillan & Bowes, and is now familiar to us as Bowes & Bowes.

Gradually theses were abolished except for doctorates, for the M.B. and as an alternative procedure for the B.D. Allbutt attached great importance to the style in which the M.B. thesis was presented and was so impressed with the inability of candidates to write decent English that he published *Notes on the Composition of Scientific Papers*, illustrated by choice examples of English as it ought not to be written. As he neatly put it, his quotations were "given for the most part without acknowledgment, for obvious reasons". Indeed, latterly he seemed more concerned about the style than the matter of the thesis. Still his efforts to stem the tide of scientific jargon, masquerading under the title of medical literature, were much needed and were not without effect.

It was complained by graduands that the delay in obtaining their degree caused by the preparation of these theses handicapped them in competing for resident appointments against graduates of other universities, or those qualified by the Conjoint Board. Allbutt met this by securing that the Bachelorship of Surgery, only obtainable when the whole M.B., B.Chir. examination had been passed, should be a registrable qualification. It was also alleged that the whole thing was stultified by literary "ghosts" who wrote the theses. But the cross-examination of the candidates would soon reveal whether the work was substantially his own, some help not being objected to. I only once had reason to be suspicious, and that curiously enough was of an M.D. thesis by a distinguished dermatologist!

It was therefore a great regret to me when my successor induced the University to abolish the M.B. thesis. I regard it as a retrograde step for the following reasons. They gave the young graduand the task of working at a specific problem and presenting his results in due form; these could be discussed with and criticized by a senior man, which should be a help to him when he later embarked on the shoals of "medical literature". It made for good personal relations for every graduand to have a talk of half an hour or so with his Regius. I owed my first personal association with Clifford Allbutt to reading my thesis to him. It induced men to revive contact with their University and College by their having to come up to read their thesis and then take their degree in person, the whole forming a pleasing ritual which distinguishes a University from a mere examining body. Since theses were abolished an increasingly large proportion of men just take the degree by proxy. To the Regius Professor the system had, besides the opportunity of knowing something of each graduate personally, the advantage of finding out just which teachers were influencing the students in the teaching hospitals. I hope I may be pardoned this incursion into controversy, which is dictated by my loyalty to my great predecessor's ideas. His efforts to raise the standard of general education of medical men were unceasing. As he said in 1902: "I have had already to observe to my pain that the Cambridge medical student of to-day is by no means 'learned'; that too often he thinks loosely, and that he does not always write even the English of the gentlemen who do the fires and murders for country journals. On his Latinity I will discreetly keep silence." It may therefore surprise some that he took so leading a part in urging, at length successfully, the abolition of compulsory Greek at Cambridge, but as he said, "If we make Greek optional we can raise our standard of Latin" and he deprecated "the sterile methods of cramming little boys with the abstract propositions of grammatical pedagogues" as a preparation for later passing the Littlego. Allbutt's own distinction as a classical scholar was recognized by his becoming President of the Classical Association and was shown by his great book on *Greek Medicine in Rome*. When this Section was established here in 1912, Osler became President and Allbutt was one of the original Vice-Presidents. It was indeed a fortunate thing for British Medicine that during most of the first quarter of this century the Regius chairs at Oxford and Cambridge were held by men of such outstanding distinction as Osler and Allbutt, so similar in outlook, so complementary in temperament. Those of us who were present at the celebration here of Osler's 70th birthday will never forget the impressive dignity and charm with which Allbutt presented the *Festschrift* to him, nor Osler's beautiful and touching reply, in the course of which he said: "To you, Sir Clifford, in fuller measure than to anyone in our generation has been given a rare privilege: to you when young, the old listened as eagerly as do now, when old, the young." It was indeed that universality of appeal which was Allbutt's great source of influence. In a sense, apart from the handicap of deafness, he never, even physically, seemed to grow old until quite shortly before his death. He could make humorous references to his years such as "that state of mind which seems mellow wisdom to its owner, but appears to the younger generation as senile obstinacy". On another occasion he said that while demonstrating

on a patient aged 40 he became conscious of a misunderstanding between himself and his students. He finally traced it to the fact that he was regarding someone as in the prime of life who to undergraduates was already in the sere and yellow leaf. In this playful humour he kept in touch with old and young alike.

It would be a misfortune for his memory if Orpen's portrait of him in the Fitzwilliam Museum should come to be regarded as an authentic likeness, for it is almost a caricature. When taxed with this Orpen replied, "Well, to tell the truth, I wasn't interested in the old man"; which is a criticism of the artist rather than of his subject.

It would be tedious to detail all the honours which fell thick on him, and all the honorary degrees conferred. It is somewhat surprising that he did not become a K.C.B. until he had been Regius Professor for fifteen years, but, as a matter of fact, he had declined a knighthood even before he was appointed to Cambridge. He had little desire for such honours, but I think he was gratified by the chorus of congratulations he received on that occasion, and also when he was made a Privy Councillor in 1920. His election to the Royal Society, now so rare for a physician, should also be mentioned.

It was delightful to enjoy his and Lady Allbutt's hospitality at St. Rhadegund's. The house and grounds are now divided up, for, alas, those spacious days are a thing of the past. After dinner his guests would discreetly retire into the garden to smoke, as for some unknown reason, tobacco fumes produced troublesome extrasystoles in their host. He had indeed several curious drug idiosyncrasies.

It was extraordinary how he managed to keep up with the doings of his old alumni. If one of them did a good piece of work he would probably receive a letter in a curious script which when deciphered would prove to be a charmingly phrased note of appreciation from his Regius Professor. Naturally, as one so interested in the history of medicine as he, Allbutt highly valued the antiquity of his office and always made use of the arms granted by Queen Elizabeth in 1590 to the Regius Professors of Physic in perpetuity. He incorporated them in his book plate; and among other cherished emblems of his office were the seal, surmounted by a small silver replica of Gian Bologna's Flying Mercury, and the actual Regius Chair of pre-Chippendale design, which together with his doctor's scarlet gown are handed on to his successors. A gesture, surely, deeply appreciated by all who value tradition and continuity.

He was a cultured scholar-physician, of a type becoming rare in these disturbed and bustling days. His fastidious taste in literature made him a meticulous critic of his own writings. They read so smoothly and pleasantly, and this he regarded as so important, that he always wrote three drafts before finally sending them to the Press. He had an almost uncanny faculty for winnowing the wheat from the chaff in the mass of new work and ideas constantly poured out.

Born before the introduction of anesthetics he had seen changes in medicine which were unrivalled and not likely to be surpassed in the future. One thing he continued to lament—the divorce of medicine and surgery. "How long", he asked, "are we to go on, as by a Solomon's Schism, cutting maladies into halves and distributing one moiety to one professor, the other to another without laughter or tears?" It is to be feared that this desirable aim is, in an age of increasing specialism, even more visionary than when he spoke.

By the force of his remarkable personality Allbutt certainly raised the status of the Regius Chair higher than it had ever been. I should like to quote some of Sir Humphry Rolleston's eloquent words about his predecessor. "Aristocratic in appearance and courtly in manner he was the most approachable of men, modest almost to a fault as towards his own attainments, enthusiastic in praise of his colleagues and juniors, and so tolerant that he seemed never to notice any small shortcomings." No wonder he was admired and beloved.

His philosophic attitude was exemplified in a letter to me a few years before his death, in which he said he knew rather than felt he was approaching the end of a long life. The last time I dined with him he said: "It isn't dying I mind; what I fear is incapacity." He was spared that, for apart from a heart attack a few months before his death, he was in very much his usual health until the fatal seizure which only lasted ten minutes. This was in the early morning of February 22, 1925, when he was nearly 89. The ultimate residue of his estate he left to Caius College for the establishment of Clifford Allbutt Fellowships for medical research.

Allbutt was a deeply religious man. A member of the Church of England, he was greatly attracted towards the Society of Friends, but as he said: "How can I leave a church in which I was born, baptized and married, with which all my life has been inextricably bound up—tendrils everywhere." It was well said of him that "among the religious he stood for scientific method; among scientists for religious faith". He preached not infrequently and sometimes in St. Edward's Church, Cambridge. Founded by the Franciscans, this tiny church with its lovely columns stands in a backwater of ancient peace, though close to the busy market place. It seems a singularly appropriate setting for one whose inward serenity remained undisturbed by close contact with outward affairs. As Archdeacon J. W. Hunkin, now the Bishop of Truro, said in his memorial sermon, "no man ever came nearer the ideal of what a Regius Professor of Physic should be in a University".

"Ripeness is All."

Section of Dermatology

President—SYDNEY THOMSON, M.D.

[October 18, 1945]

Angioma Serpiginosum (Crocker).—J. E. M. WIGLEY, M.B.

Miss R. M., aged 35.

The original area on the right upper arm was first noticed about twenty years ago. This has spread to its present distribution within the last four to five years and new lesions are still appearing. None of the lesions is known to have disappeared spontaneously. There are no symptoms associated with it, but the patient is distressed by its appearance. Her general health and bodily functions are unaffected. She does not take any drugs, such as adalin, &c.

The distribution is shown in fig. 1 and will be seen on the arms, trunk and thighs, being more marked on the right side than on the left. Note the sharp line of demarcation down the mid-trunk. The essential appearance is well shown in fig. 2. It consists of a reticular and partly serpiginous telangiectasia of varying intensity, dotted over with bright red "cayenne pepper" spots, some of which feel raised above the surface but do not disappear on pressure. There is no pigmentation visible. No scaling or definite atrophy of the skin was obvious. Two rectangular areas, shown in the photograph, were treated with a radium plaque about two years ago, where it will be seen that the lesions have almost disappeared.

Histology.—Sections were made and examined by Dr. Freudenthal who writes that the essential changes were a number of very considerably dilated capillary vessels in the papillary body, mostly filled with red blood corpuscles, and that there was hardly any cellular infiltrate. This is in contrast to the picture usually seen in Schamberg's disease and agrees well with the diagnosis of angioma serpiginosum.

It appears that the case is typical of that described by Sir Jonathan Hutchinson ("A Peculiar Form of Serpiginous and Infective Nævoid Disease", *Arch. Surg.*, 1890, 1, Part 9). The name angioma serpiginosum was later given to the condition by Radcliffe Crocker ("Angioma Serpiginosum". *Diseases of the Skin*, 1905, 2, 906).

Is it the view of members that thorium X would be the best method of treatment?

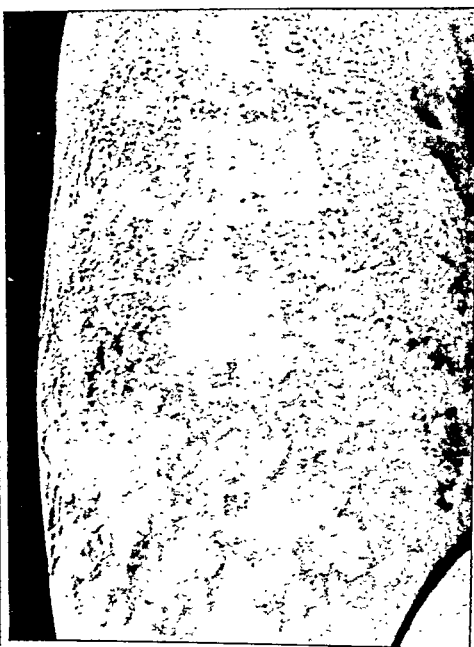
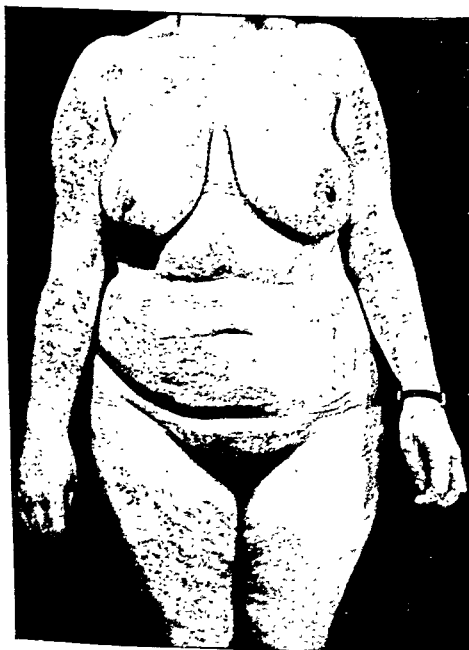


FIG. 1.

Angioma serpiginosum. (Photographs by A. C. Roxburgh, M.D.)

FIG. 2.

Dr. H. C. Semon: Thorium X is well worthy of trial, the more so because there is no other treatment available.

Dr. F. Parkes Weber: I do not see any other way of treating this case than by making the small blood-vessels atrophy. This is apparently what has happened to the area on one shoulder which is now free as a result of previous radium exposure. These cases vary in degree. There may be very slight cases with just a line of red or cayenne pepper spots. I had two cases together many years ago (F. P. Weber, *Proc. R. Soc. Med.*, 1927, 20, Sect. Derm., 107) and spontaneous involution has taken place since then in at least one of the two cases. The condition is certainly developmental, but apparently seldom if ever familial (see, however, Williams, *Arch. Derm. Syph.*, Chicago, 1924, 9, 783).

Dr. W. N. Goldsmith: I have had success with ultraviolet rays.

Poikiloderma Atrophicans Vascularis.—H. MACCORMAC, C.B.E., M.D., and J. E. M. WIGLEY, M.B.

H. T., a man aged 41 years, a Polish national, was seen by one of us (H. MacC.) on October 3, 1945. He stated that the eruption first appeared on the flexural regions of the arms at 19 years of age and has gradually extended and continued up to the present time. The condition worsened last year, when he was admitted into Ashridge E.M.S. Hospital under Dr. Wigley. The patient is an unusually well-built man without any trace of muscular affection. He has been treated for a duodenal ulcer and has spent during the war six months in India. His blood-count is normal and the blood Bordet-Wassermann reaction is negative. Temperamentally he is highly-strung which may account for the complaint of cramp in the arms, a symptom elicited by a leading question.

The eruption is widely distributed as follows: the skin of the cheeks is lightly pigmented and possibly atrophic; on the neck there is a collar of reticular pigmentation, while over the arms and breasts pigmentation, dilated vessels, desquamative and finely atrophic skin are observed. In the region of the groins there is a reticular pigmentation similar to that seen on the neck, while over the thighs, fading as it extends downwards on to the legs, the skin is bright reddish-blue, with atrophy, slight scaling, and marked capillary dilatation. The resemblance to X-ray dermatitis which has been often remarked upon is well shown in this case.

A number of examples of this rare disease process have been exhibited at the Section during the last fifteen years and have been fully reported. Until the valuable and illuminating paper by G. B. Dowling and W. Freudenthal (*Brit. J. Derm.*, 1938, 50, 519) appeared, it would seem that dermatomyositis and poikiloderma atrophicans vascularis were often confused both here and abroad, and dermatology owes a debt to these authors for giving us the measure, clinical and histological, by which these two conditions can be distinguished. On this evidence it would seem that the original case described by Petges and Cléjat should now be classified as dermatomyositis. The histological differences have been summarized by Dowling and Freudenthal as follows: in poikiloderma the changes are characteristic of inflammation, in dermatomyositis they are degenerative; and the inflammatory character of the reactions in a section from the case now under consideration bears this out.

Dr. F. W. Jacobson: Dr. Mitchell Heggs and I in a case similar to this some years before the war carried out treatment by thorium X (*Proc. R. Soc. Med.*, 1936, 29, 717-720 (Sect. Derm., 57)). I was able to follow up the case for years. Thorium X was given once a fortnight—1,500 electrostatic units. The irritation disappeared completely, the pigmentation also disappeared. The atrophic changes were not altered. From this point of view it should be tried in this case as well.

Dr. H. MacCormac: Is it meant that the whole affected area should be painted with thorium X, i.e. most of the body surface?

Dr. F. W. Jacobson: Yes, it takes a long time to show a good result.

Dr. H. MacCormac: What is the effect on the blood?

Dr. F. W. Jacobson: No effect.

Pityriasis Lichenoides et Varioliformis.—ALICE CARLETON, M.D.

Male child aged 3, with a diffuse rash on the body and limbs, consisting of pinkish-brown macules with slight scaling, crusted vesico-papules about $\frac{1}{8}$ inch in diameter, pitted scars and patches of pale atrophic skin on the forearms. The rash and blood-count are normal. He has carious incisors and enlarged cervical and axillary glands. The condition has existed for a year. In view of the duration of so many of these cases, is the term "acuta", which is generally added to the title, a suitable one?

Dr. G. B. Dowling: A case which I presented at a recent meeting pursued a course of about three months from beginning to end.

Dr. H. W. Barber: I agree with Dr. Dowling. I have seen one case—the wife of a doctor—in which the eruption disappeared in about a month. She had injections of gold, but

I cannot say whether they had any effect. The duration of the disease admittedly varies greatly. The same is true of the cases without varioliform lesions, of which Dr. MacCormac first showed an example at this Section.

Dr. A. C. Roxburgh: I had a case in a soldier who came to Bart's during the war. He had had the condition all through the war and it had been possible to keep it in check to some extent by ultraviolet light, but it did not entirely clear up.

‡ **Kaposi's Angiosarcoma.**—ELIZABETH HUNT, M.D.

Married man, aged 47. First became aware of a red spot on the skin of his back two years ago. Since then it has gradually developed into the present condition. It has never caused him any discomfort, except for slight irritation at times. He has no clear recollection of ever having had any injury at the site.

The area now affected extends laterally to the left for about 10 to 12 inches from the lower dorsal and lumbar spines.

The lesions are raised indurated tumours, the surfaces of which are elephantiasic in appearance or in some parts resemble hæmangiomas.

At the borders of the area, narrow red inflammatory-looking curved lines are present, which are infiltrated.

Pathological Report (Dr. Janes):

W.R. negative.

Corrected sedimentation rate 8 mm.

Hæmoglobin 110%

R.B.C. 5,510,000 per c.mm.

C.I. 1.0.

W.B.C. 7,400 per c.mm.

Differential count:

Polys. 66%

Lymphos. 19%

Monos. 13%

Eosinos. 2%

Histology.—There is a dense proliferation of spindle cells in the corium around small capillary-like spaces, accompanied by patchy lymphocytic infiltration. The overlying epithelium is not involved in the process. I feel that the spindle cells are vasoformative in origin and the presence of mitoses as well as the general features suggest an angiosarcomatous structure. This conclusion raises the question of Kaposi's disease.

Sections stained for iron showed no iron present.

Dr. H. W. Barber: I showed a case of this kind some years ago in an elderly man. There is always a discussion as to whether these cases are mycosis fungoides of the "d'émblée" type, or true sarcomata. My own opinion is that they are sarcomata. The serpiginous and infiltrated erythematous lesions surrounding the tumours are an interesting feature and recall those seen in the so-called "carcinoma erysipelatoides".

Dr. F. Parkes Weber: Are there not some cases in which lines like those in the present case referred to by Dr. Barber occur on the skin in patterns? I think I have seen illustrations described as pre-mycotic cases, but of course pre-mycotic eruptions, if really infiltrated, are cases of true mycosis fungoides, and the mass in the present case may be mycosis fungoides d'émblée.

Dr. G. Dowling: I doubt whether it is always possible clinically to distinguish between mycosis fungoides a tumeur d'émblée and sarcoma of the skin. A certain histological picture belongs to mycosis fungoides and another to sarcoma. I do not believe either that it is possible to estimate the prognosis; some may be controlled for years by X-ray, while others pursue a rapidly malignant course with involvement of organs or bone.

Dr. A. C. Roxburgh: I showed a case very much like this to the British Association of Dermatology in 1942. I had shown it as mycosis fungoides, but it was taken clinically by most members to be probably a sarcoma. A section was made, and it proved to be some form of sarcoma. I turned the patient over to the X-ray therapy department at Bart's and they gave him treatment. He has kept well since.

Dr. H. W. Barber: Have members seen the lesions in these cases break down ultimately? The case, to which I have just referred, was treated with X-rays over a long period, and some of the nodules broke down and ulcerated.

The President: I have seen one case break down—histologically it was most like a fibrosarcoma.

Dr. C. H. Whittle: Does the response to X-rays help in distinguishing between mycosis fungoides and sarcoma?

The President: These merging types are both very radio-sensitive.

Dr. W. N. Goldsmith: We have to consider the significance not only of responsiveness to X-rays, but also of spontaneous disappearance. Some cases that begin like mycosis fungoides clinically and histologically, the lesions of which from time to time vanish of their own accord, develop later into a condition indistinguishable from sarcoma, which is steadily progressive and fatal. Pathologists as well as clinicians may have difficulty in drawing the line between mycosis fungoides and sarcoma; and analogously, as Ferguson Smith has pointed out (1934, *Brit. J. Derm.*, 46, 267), even lesions with the histology of prickle-celled carcinoma may heal spontaneously.

Dr. W. Freudenthal: I agree with Dr. Goldsmith that sometimes neither clinically nor histologically are we able to draw a line between mycosis fungoides and this kind of sarcoma.

Benign Lymphogranuloma of Schaumann with Apparent Involvement of the Anterior Pituitary.—H. W. BARRER, M.B.

Mr. O. S., medical student. Native of Honduras. Aged 28. Resident in this country for over six years. He was referred to me by Dr. Mumford in January 1945, after having been under his and Dr. Savarard's care for some time. He had been treated with injections of gold and sodium morrhuate without apparent improvement of any note, but the amount given of both appears to have been small.

This case is chiefly of interest in that the patient at one time presented a syndrome of symptoms indicative of involvement of the anterior part of the pituitary gland, presumably owing to infiltration by a nodule of sarcoidosis.

There is nothing of note in his previous medical history, except that he has had benign tertian malaria. Both his parents and three sisters are alive and well.

Résumé of history of the sarcoidosis.—Onset (probably about five years ago): The first symptom was swelling and tenderness of the terminal part of the right ring finger. Subsequent X-ray examination showed that the greater part of the terminal phalanx had disappeared. He was advised to go away for three months, and on his return another radiograph revealed that there had been regeneration of bone, but the finger remained swollen and tender.

During the following winter, acute and very painful swelling, lasting about ten days, of finger- and toe-joints occurred, but only one joint was affected at a time. A diagnosis of arthritis was made, and injections of gold were given, but these afforded only temporary improvement, and the condition of the fingers and toes deteriorated every winter.

At the beginning of 1944 an increasing asthenia was experienced and shortly afterwards the first lesions of the skin appeared, first on the forehead, and later on the cheeks, eyelids, nose, and lobes of the ears. The appearance of the nodules on the nose was preceded by intense itching and vascular dilatation.

Asthenia: Slight at the onset, became severe at the beginning of 1944, so that he could hardly rise in the morning and was utterly exhausted by the end of the day. By September 1944 he felt too ill to leave his house. With the asthenia there developed almost complete loss of appetite, and of libido and sexual potency.

Loss of body hair: In July 1944 he observed the disappearance of coarse hair from the arms, legs and axillæ, and marked thinning of the hair in the pubic region.

COMMENT.—I first saw the patient 4.1.45 and he was admitted to Nuffield House, Guy's Hospital 7.2.45. The main features then were:

Skin: Large numbers of sarcoid lesions of various types on the forehead, cheeks, nose and ears. The nose presented the appearance of lupus pernio. One lesion on the abdomen and one on the left leg.

Bones and articular structures: The terminal and first interphalangeal joint-areas of all the fingers and both thumbs were involved. The toes were similarly affected.

Glands of considerable size were palpable in the cervical region, and the epitrochlear ones were noticeably large.

Body hair: No coarse hair on the arms, legs, and in the axillæ. Pubic hair scanty.

The skin as a whole was dry, and presented the "flaky" appearance seen in Simmonds' disease. There was very marked keratosis pilaris.

Blood-pressure varied from 90/60 to 100/70.

Dr. Bishop saw the patient with me and agreed that the symptoms suggested involvement of the anterior part of the pituitary gland. There has also been evidence of diabetes insipidus, which has been recorded in this disease by Léné, Launay et Séc (*Société Méd. des Hôp. de Paris*, 1935, 1137), by Tillgren (*Brit. J. Derm.*, 1933, 47, 223) and by Snapper, in that he had marked polydipsia and polyuria, which developed in 1944 at the same time as his loss of appetite, and continued until soon after he entered hospital.

The reports on the various investigations are appended.

Report on the eyes by Mr. Frank Law: There is evidence of a low-grade chronic cyclitis in the form of large keratitis punctata spots; these are of the greasy, "mutton-fat" variety, commonly associated with a tuberculous infection of the eye. Some secondary vitreous haze.

Treatment.—Dr. Bishop agreed that replacement therapy should be attempted for the pituitary deficiency, and he implanted under the skin 200 mg. of desoxycorticosterone acetate and 600 mg. of testosterone on 24.2.45.

Dried thyroid 1-1½ grains daily was taken from 25.4.45 to 7.6.45.

For the sarcoidosis I decided to try the effect of stovarsol: 6 grains were given after breakfast and 4 grains in the evening for three successive days, followed by three days' interval. He had 13 courses of stovarsol between 2.3.45 and 14.6.45. He also received two blood transfusions, a course of intramuscular injections of plexan, and iron by mouth; and for a while exposures of ultraviolet light.

A second implantation of desoxycorticosterone acetate and testosterone was also made. He has been away from hospital for short periods, but has now been readmitted.

Result of treatment.—There has been a marked improvement in the sarcoidosis. Many of the lesions on the face have cleared up, leaving stains. Those of the nose and ears have greatly diminished in size, and the fingers and toes are less swollen and congested.

As regards the involvement of the anterior pituitary, the patient has recovered his vigour and appetite, and coarse hair has regrown on the limbs and pubic region and in the axillae. The general texture of the skin is now normal and the blood-pressure is 110/70.

—I doubt whether the improvement is entirely due to replacement therapy. It seems more likely that the pituitary gland has recovered its function—at any rate to some extent.

Radiograms.—Chest: The hilar shadows are large and dense and there is a calcified focus on the right with a thickened right interlobar septum. There is in addition an increase of striation to the right upper lobe and while no definite focus is noted the presence of active tubercle cannot be excluded.

Skull: The pituitary fossa is rather shallow but of normal A.P. length. The posterior clinoids are larger than normal with a thin line of calcification connecting them to the anterior clinoids. There is in addition some calcification of the clino-petrous ligament.

Bones: Marked decalcification of phalanges of the feet and hands, with areas of complete bony absorption and some narrowing of interphalangeal joints.

Serum proteins: Total, and A/G ratio normal.

Serum sodium and chloride: Both low at first. Improved after additional salt in diet for a while, but were low again 12.10.45.

Urine: Sp. gr. 1006, pH 6.0. Nil abnormal found.

Blood: Numerous blood-counts and estimations of the B.S.R. were made. The main features were polynuclear leucopenia; eosinophilia, which varied greatly (highest 15%); moderate diminution of hæmoglobin, which improved after blood-transfusions; and moderate increase of B.S.R.

? **Reticulosis.**—LOUIS FORMAN, M.D.

Married woman, aged 30. Ten months ago was delivered of a macerated fœtus (6 months). Two years' history of grouped papules over abdomen, upper thighs, and fronts of shoulders. The central brown papule, 3-4 mm. in diameter, tended to necrose in the centre, and was surrounded by smaller, flat, brown papules.

Section of a larger papule shows an infiltration in the cutis consisting of cells with irregular large nuclei and and some giant cells: strongly suggestive of a reticulosis.

Blood-count (September 20, 1945).—Hb. 67%; R.B.C. 3,960,000; W.B.C. 5,300. Polys. 37%; lymphos. 58.5%; monos. 4%; eosinos. 0.5%.

Favus.—H. J. WALLACE, M.D.

Girl, aged 16, with a history of recurrent sepsis and crusting in the scalp for the past three years. No diagnosis was made originally, though some of the lesions bore some resemblance to psoriasis. Recently atrophy and scutula appeared. The condition began when she was evacuated to Berkhamsted. Four other young children are at home, with no evidence of infection. Fungus is present in the hair on microscopical examination and a culture is being made.

The President: These cases of favus are extremely interesting and I feel reasonably certain that twenty or twenty-five years ago we did not have cases of this type at all, yet there is no doubt that now we are all beginning to see these cases which suggest psoriasis, so that at first the possibility of fungus infection does not occur to one.

Dr. C. H. Whittle: I collected notes of cases which various members had shown before and mentioned them with my own three cases at the meeting of the British Association of Dermatology last July. My impression was that quite a number of them had recovered. In discussing diagnosis and treatment with Dr. A. M. H. Gray, I learnt that he had had

Dr. W. Freudenthal: I agree with Dr. Goldsmith that sometimes neither clinically nor histologically are we able to draw a line between mycosis fungoides and this kind of sarcoma.

Benign Lymphogranuloma of Schaumann with Apparent Involvement of the Anterior Pituitary.—H. W. BARBER, M.B.

Mr. O. S., medical student. Native of Honduras. Aged 28. Resident in this country for over six years. He was referred to me by Dr. Mumford in January 1945, after having been under his and Dr. Savatard's care for some time. He had been treated with injections of gold and sodium morrhuate without apparent improvement of any note, but the amount given of both appears to have been small.

This case is chiefly of interest in that the patient at one time presented a syndrome of symptoms indicative of involvement of the anterior part of the pituitary gland, presumably owing to infiltration by a nodule of sarcoidosis.

There is nothing of note in his previous medical history, except that he has had benign tertian malaria. Both his parents and three sisters are alive and well.

Résumé of history of the sarcoidosis.—Onset (probably about five years ago): The first symptom was swelling and tenderness of the terminal part of the right ring finger. Subsequent X-ray examination showed that the greater part of the terminal phalanx had disappeared. He was advised to go away for three months, and on his return another radiograph revealed that there had been regeneration of bone, but the finger remained swollen and tender.

During the following winter, acute and very painful swelling, lasting about ten days, of finger- and toe-joints occurred, but only one joint was affected at a time. A diagnosis of arthritis was made, and injections of gold were given, but these afforded only temporary improvement, and the condition of the fingers and toes deteriorated every winter.

At the beginning of 1944 an increasing asthenia was experienced and shortly afterwards the first lesions of the skin appeared, first on the forehead, and later on the cheeks, eyelids, nose, and lobes of the ears. The appearance of the nodules on the nose was preceded by intense itching and vascular dilatation.

Asthenia: Slight at the onset, became severe at the beginning of 1944, so that he could hardly rise in the morning and was utterly exhausted by the end of the day. By September 1944 he felt too ill to leave his house. With the asthenia there developed almost complete loss of appetite, and of libido and sexual potency.

Loss of body hair: In July 1944 he observed the disappearance of coarse hair from the arms, legs and axillæ, and marked thinning of the hair in the pubic region.

COMMENT.—I first saw the patient 4.1.45 and he was admitted to Nuffield House, Guy's Hospital 7.2.45. The main features then were:

Skin: Large numbers of sarcoid lesions of various types on the forehead, cheeks, nose and ears. The nose presented the appearance of lupus pernio. One lesion on the abdomen and one on the left leg.

Bones and articular structures: The terminal and first interphalangeal joint-areas of all the fingers and both thumbs were involved. The toes were similarly affected.

Glands of considerable size were palpable in the cervical region, and the epitrochlear ones were noticeably large.

Body hair: No coarse hair on the arms, legs, and in the axillæ. Pubic hair scanty.

The skin as a whole was dry, and presented the "flaky" appearance seen in Simmonds' disease. There was very marked keratosis pilaris.

Blood-pressure varied from 90/60 to 100/70.

Dr. Bishop saw the patient with me and agreed that the symptoms suggested involvement of the anterior part of the pituitary gland. There has also been evidence of diabetes insipidus, which has been recorded in this disease by Léné, Launay et Sée (*Société Méd. des Hôp. de Paris*, 1935, 1137), by Tillgren (*Brit. J. Derm.*, 1933, 47, 223) and by Snapper, in that he had marked polydipsia and polyuria, which developed in 1944 at the same time as his loss of appetite, and continued until soon after he entered hospital.

The reports on the various investigations are appended.

Report on the eyes by Mr. Frank Law: There is evidence of a low-grade chronic cyclitis in the form of large keratitis punctata spots; these are of the greasy, "mutton-fat" variety, commonly associated with a tuberculous infection of the eye. Some secondary vitreous haze.

large circumscribed masses of closely packed epithelioid cells surrounded by a very thin zone of lymphocytes. (This was reported by Dr. Muende.)

Before the results of the investigations were known she was given potassium iodide, 10 grains, t.d.s., without any helpful effect. She has made a marked improvement following the administration of arsenic trioxide, grain 1/50, one, t.d.s.—160 tablets in all.

Epidermolysis Bullosa.—GEOFFREY DUCKWORTH, M.R.C.P.

Miss J. B., aged 17. For the past eleven months has been troubled by the development of vesicles and bullæ on only slight traumatic provocation. The back of the hands is the part particularly affected, but she has some macular and papular lesions on the front of the legs. She also has acne vulgaris (with exaceriations) of the face and back and some of the papules readily form vesicles, and occasionally bullæ. There are many purplish patches of skin representing the sites of former lesions.

Her father and his brother have suffered from attacks of similar vesicles and bullæ following slight injury, but the attacks began only in manhood and do not last for more than about six months at a time.

Examination of the fluid from a typical bulla was negative for organisms, and cultures were sterile.

Treatment, which has included ascorbic acid and vitamin-P, and small doses of thyroid, has not had any demonstrable effect.

Dr. F. Parkes Weber: I think that Dr. Duckworth's case belongs to a variety of epidermolysis bullosa more or less completely localized to the hands or feet or both hands and feet, characterized by a recurrent bullous eruption in summer, the exciting cause being the hot weather more than local traumatism. The familial incidence is very striking, as first pointed out by E. A. Cockayne (*Brit. J. Derm.*, 1938, 50, 358), who, however, could find only one similar case recorded, namely, that in a boy aged 4 years, by F. Parkes Weber (*Proc. R. Soc. Med., Section Dermat.*, 1926, 19, 72). This boy is still troubled in exactly the same way in summer; the bullous eruption on his feet during summer makes standing painful and work in the R.A.F. became practically impossible. In this case I could obtain no family history of any similar condition. I have recently been told of another case in a boy, aged 6 years, whose father has always had the same tendency to get bullæ on the feet in summer. Rubbing is said to favour the development of the bullæ. There have been many reports in America on this "Cockayne" or "Weber-Cockayne" bullous eruption—see especially M. Waisman, "Recurrent Bullous Eruption of the Feet and Hands (Weber-Cockayne)—Localised Epidermolysis Bullosa", *J. Amer. med. Ass.*, 1944, 124, 1247, containing many references to the recent literature; see also J. B. S. Haldane, "A New Pedigree of Recurrent Bullous Eruption of the Feet", *J. Heredit.* (Baltimore), 1942, 33, 17.

I realize that the case shown by Dr. Duckworth to-day cannot as yet be classified as a typical example of the above variety of epidermolysis bullosa. Longer observation is required, together with exact details of the bullous eruption as it affected her relatives. It may have been more typical in these relatives.

Dr. Duckworth: I am much obliged to and thank Dr. Parkes Weber. This girl, however, developed her trouble last winter.

Dr. Parkes Weber: The case is certainly as yet altogether atypical, and the progress of the case as well as more exactness in the family history must decide the diagnosis.

Non-diabetic Necrobiosis Lipoidica.—G. B. DOWLING, M.D.

Woman aged 60. She says that the condition, which began in 1916, looked like a mosquito bite at first. From that time it has very gradually enlarged, extending by a solid thin cord-like edge, leaving in its wake a very special kind of delicate waxy scar through which veins are seen to course as clearly as in atrophoderma of the Pick-Hersheimer type. I first knew this patient twenty years ago, when the lesion looked just as it does now except that it now covers about three times the area that it did then, and part of the granulomatous edge has disappeared. A section made then showed that this growing edge had a tuberculoid structure. The case was exhibited with the diagnosis of ? sarcoid. Subsequently Dr. Goldsmith presented a similar case with the diagnosis of morphaea-like tuberculide; necrobiosis lipoidica had not yet been described. Dr. Wallace has presented two exactly similar cases

Dr. W. Freudenthal: Does Dr. Dowling think that the diabetic and the non-diabetic form might show clinical differences?

Dr. G. B. Dowling: I brought the case here really with the object of asking the question which Dr. Freudenthal has just put. I wondered whether these cases, with their extremely characteristic tuberculoid edge and waxy centre, might not be unrelated to the diabetic necrobiosis lipoidica.

Dr. W. N. Goldsmith: I cannot distinguish between diabetic and non-diabetic cases.

similar cases which he had been treating successfully with X-ray epilation, though some required a second epilation before final cure. I think they were mostly fairly early cases.

Multiple Chronic Ulcers of the Upper Trunk in a Young Woman. ? Acne Conglobata.—C. H. WHITTLE, M.D.

M. T., aged 22, a W.A.A.F. Three years' history of ulcers on the back and shoulders. Each ulcer takes two to three months to develop and heal. The first was on the shoulders. The latest was removed from left lower dorsal region for microscopy. Previous history good. Family history nothing relevant. There are now four fairly active lesions; one 1 in. diameter on left shoulder, bluish-red—mostly healed over but with a few pustules lying deeply on the edge. There are about 35 scars, oval or round, varying up to 5/8 in. diameter chiefly around the shoulder but also over the dorsal region, many showing a tendency to keloid.

There is a close similarity between the scars and smaller active lesions in my second case.

Wassermann and Kahn negative. Culture: *Staph. aureus*. Mantoux: 1:1000 Human ++; 1:1000 Bovine+.

Chest X-ray: No abnormality.

Biopsy: Shows ulceration and granulation tissue containing plasma cells, endothelial-type cells, and small round cells; polymorphs are present in places. The picture does not suggest nor does it exclude tubercle. [Section was shown.]

Multiple Chronic Ulcers of the Arms and Trunk. ? Cause.—C. H. WHITTLE, M.D.

D. H., aged 60. A ditcher. Twenty-five years' history of ulcers on the arms and upper trunk. Besides the large active but indolent ulcers on the upper arms there are very large numbers of oval or circular scars of healed ulcers on the back.

This case was shown earlier in the year (*Proc. R. Soc. Med.*, 1945, 38, 502). Since then penicillin intramuscularly has been tried without success, though a penicillin-sensitive *Staph. aureus* was obtained on several occasions from the lesions. No blastomyces have ever been seen or grown.

Recently, X-rays have been given a trial and he has had four doses of 200 r (Dr. Japha) to the lesion in the centre of the chest, which is now healing. He attributes the healing to the treatment.

Compare these lesions with those in my previous case of a young woman with three years' history of somewhat similar indolent ulcers.

COMMENT.—I am indebted to Dr. Duckworth for the suggestion that the ulcers might be due to anaerobic streptococci, and we have obtained some anaerobic streptococci in the last day or two from the man's unbroken pustules.¹ Whether that is going to be an important factor or not I do not know. The suggestion of tubercle has been put forward, but I have not found any evidence. A third suggestion has been artefact. One must not rule out artefact, I suppose, in long-standing cases of this sort, but to my mind, considering the temperament of both these patients, it is unlikely. The girl is intelligent and attractive, and I should have thought she was able to impress her personality in other more agreeable ways. The position of the lesions is also against that supposition. The man has had ulcers since he was 35; he is now 60, and he did not consult anyone about it until the last month or two, when he saw a doctor. They did not interfere with his work. I think the circumstances are against the idea that these lesions were designed to attract sympathy to himself.

The President: I have had one case where zinc peroxide had a certain effect, but a much better effect was obtained with a 2½% Milton. These cases in my experience have a very long history, and even when healed up, they relapse again some months later.

Circinate Sarcoids of the Face and Limbs.—GEOFFREY DUCKWORTH, M.R.C.P.

Mrs. M. C., aged 37, a cook. Nineteen months ago developed a bluish-red eruption chiefly on the arms and forearms, and legs, with isolated lesions on the sides of the face. When seen in June 1945 the lesions consisted of dusky rings, which had diameters varying from a half to several inches. The borders were mostly serrated, and not obviously raised. The centres of the lesions consisted of normal skin, or very slight atrophy. The lesions looked sub-epidermal.

A W.R. and a Kahn test were negative. A histological section shows the presence of

¹ POSTSCRIPT. (14.9.45).—The streptococcus has been grown in pure primary culture, has micro-aerophilic characters and gives some of the reactions of a hæmolytic enterococcus. The examination by Dr. A. I. H. Tomlinson is not completed.

active lupus of the lobe of the left ear and adjacent skin, still mildly active and showing nodules. She had not had treatment of any kind for many years. I first saw her in July 1944 and gave her calciferol, 150,000 i.u. daily. By September 1944 the lesions were showing obvious response and the dose was reduced to 100,000 i.u. daily. The lupus continued to regress slowly and she was kept on this dose until August 1945, when it was further reduced to 50,000 i.u. daily, which she is still taking. The glabellar lesion is now quite flat and shows mainly residual staining. There is still slight activity in the lower portion of the lesion. The ear lesions have completely healed and no nodules can be found. Her serum calcium level on October 31, 1945, was 10.5 mg. per 100 c.c. She has never been upset by the drug.

CASE IV.—Arthur M., aged 41. Extensive sheet of lupus on upper and inner aspect of right thigh, slowly progressive. Whole area thickened and raised, dusky red and rather scaly, resembling widespread lichenification. Section showed typical tuberculous structure. No previous treatment of any kind.

January 2, 1945: Given calciferol, 150,000 i.u. daily. At the end of the month the lesion showed response, being flatter and paler.

February 12, 1945: Dose reduced to 100,000 i.u. daily. Continued on this until August 13, 1945, since when he has been taking only one dose daily of 50,000 i.u. Serum calcium level on June 25, 1945, was 10.6 mg. per 100 c.c. By October 29, 1945, the whole lesion was flat, with residual pigmentation and islands of pink, clear, slightly atrophic skin. Serum calcium on that date: 10.1 mg. per 100 c.c. No intolerance to drug.

CASE V.—Mrs. Elizabeth G., aged 65. First seen December 12, 1943, with superficially ulcerative lupus of bulbous portion of nose and nasal vestibules of eight years' duration. She was treated until April 1944 with applications of liquid acid nitrate of mercury and radiostoleum by mouth with some response. Was then given calciferol, 100,000 i.u. daily until December 1944, when she ceased attending of her own accord because her nose had improved so much that it did not worry her any more. No intolerance to drug.

July 1945: No clinical lupus.

October 1945: Well. Serum calcium 11.2 mg. per 100 c.c.

CASE VI.—George Y., aged 45. Lupus involving whole of left ear and adjacent skin, twenty years' duration. More recent patch left malar area. All lesions active, with ulceration and crusting along helix.

First seen May 4, 1945. Confirmatory biopsy (left side neck). Calciferol given, 100,000 i.u. daily and continued ever since.

July 9, 1945: Good response. No further crusting and ear thinner and softer. Biopsy (apex of pinna, to exclude epithelioma because of thickening): Tuberculous histology.

Serum calcium, August 14, 1945 (after 100,000 i.u. calciferol daily approx. three months): 10.8 mg. per 100 c.c.

October 29, 1945: All lesions practically healed except for apex of pinna which is still crusting and slightly infected. No intolerance to drug at any time.

Of the other thirty-two cases, demonstrable improvement of varying degree has occurred in twenty-one cases, viz. of the total number of thirty-eight cases in which calciferol has been tried, there has been a favourable response in twenty-seven (approximately 71%). As regards the remaining eleven cases, in some calciferol has produced little appreciable change; in others, its effect has been difficult to assess, either because the lupus has more or less burned itself out or has become masked by previous scar-producing treatment of one kind or another, or by chronic radiodermatitis. Amongst the first-mentioned was the case of a child, a girl aged 10, who had a single small plaque of lupus in the right cheek of about one year's duration. We gave her calciferol, 50,000 i.u. daily for two months, at the end of which the lesion appeared a little flatter and paler. However, in view of the poor state of her general health we decided she needed full institutional treatment and arranged for her admission to the Treloar Home at

[November 15, 1945]

Lupus Vulgaris Treated with Calciferol

By G. B. DOWLING, M.D., and E. W. PROSSER THOMAS, M.D.

Dr. Prosser Thomas: We are presenting these cases of lupus vulgaris because of their good response to the oral administration of calciferol as virtually the only form of treatment. We have been treating lupus with calciferol since 1943. Including the six cases shown here to-day, we now have records of thirty-eight lupus patients who are being treated exclusively with calciferol or being followed up after stopping it.

It was Dr. Dowling who began giving calciferol in lupus, and the first patient to be treated with it is among those demonstrated to-day. [Case I.]

CASE I.—Sidney B., aged 30. This man was attending St. Thomas's Hospital with confluent lupus of the face. He had been receiving intensive treatment elsewhere for the previous five years, including daily carbon arc baths and applications of Finsen light two or three times a week. He had also had injections of Alepol and of N.A.B. His lupus, however, which had begun near the right ear when he was 20, had steadily extended and for the past nine months his whole face had been in a congested and œdematous state and showed no signs of subsiding. In August 1943, Dr. Dowling began giving him calciferol, 50,000 i.u. three times a day in tablet form. After taking these for a few days he said that he developed nausea and felt generally ill and had to go to bed. His face got worse, the congestion increasing and exudation began. He discontinued the calciferol and stayed in bed for a fortnight. By then the congestion had subsided and he noticed that his lupus had improved, so much so that he began taking the calciferol again of his own accord. In a month or so, however, he had a second flare-up in the face, associated with general malaise, though less severe. He again discontinued the calciferol temporarily. He has tolerated the drug well ever since, except for occasional slight "stomach disorder". His lupus continued to regress and after a few months the dose of calciferol was reduced to 50,000 i.u. twice daily. By July 1945 there were only two rather doubtful lupus nodules to be found; his skin otherwise was comparatively clear and showed only soft and very superficial scarring. The calciferol was then reduced to one dose of 50,000 i.u. a day, on which he continued until October 30, 1945, when he was taken off it altogether. His serum calcium on that date was 14.8 mg. per 100 c.c. Apart from the two questionable nodules in the right cheek, which have remained unchanged for some months, his lupus appears to have cleared completely.

CASE II.—Miss Jane P., aged 71, another of the cases presented to-day, was of a very similar congested type. She had had lupus for about five years. Her whole face, like that of Dr. Dowling's patient, had become distressingly angry and swollen and there was superficial ulceration of the cheeks, nose, and upper lip. The nasal mucosa was also involved, and the septum perforated. I first saw her in November 1944 and put her on calciferol, 150,000 i.u. daily, together with zinc cream and soluble sulphacetamide 5% to use as nasal plugs so as to try and clear up the secondary infection in the nose, which was practically blocked up with crusts. Her skin showed rapid response and by March 1945 was virtually clear, as it is to-day. She discontinued calciferol at that time and has shown no signs of relapse. The drug has never upset her.

CASE III.—Miss Emma C., aged 72. In contrast to the above two acute forms of lupus, this patient had a large plaque of lupus tumidus in the glabellar area, which had been present without appreciable change for about thirty years. She also had superficially ulcer-

active lupus of the lobe of the left ear and adjacent skin, still mildly active and showing nodules. She had not had treatment of any kind for many years. I first saw her in July 1944 and gave her calciferol, 150,000 i.u. daily. By September 1944 the lesions were showing obvious response and the dose was reduced to 100,000 i.u. daily. The lupus continued to regress slowly and she was kept on this dose until August 1945, when it was further reduced to 50,000 i.u. daily, which she is still taking. The glabellar lesion is now quite flat and shows mainly residual staining. There is still slight activity in the lower portion of the lesion. The ear lesions have completely healed and no nodules can be found. Her serum calcium level on October 31, 1945, was 10.5 mg. per 100 c.c. She has never been upset by the drug.

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Alton. This was the only case in which we have had an opportunity of trying calciferol in lupus in childhood and in an early stage.

COMMENT

Calciferol (vitamin D₂) is a potentially toxic drug. It is a purely artificial substance, prepared by exposing the vegetable sterol, *ergosterol*, to ultraviolet light. It is said to be almost always contaminated with other possibly toxic by-products of irradiation, and to be more toxic than the naturally occurring vitamin D₃, which is found in animal products such as egg-yolk, butter, and fish liver oils, and is derived from irradiated animal sterols (Bicknell and Prescott, 1942).

Though apparently never tried hitherto in lupus, calciferol has been used in a variety of other diseases, often in very high dosage, and toxic symptoms have been observed not infrequently and reported in the literature. General well-being and a good appetite are said to be often the first symptom of poisoning. Anorexia may follow, together with nausea, vomiting, diarrhoea, and polyuria. Mental depression and headache may be early symptoms. Excessive doses mobilize phosphorus and calcium, thus broadly having an opposite effect to normal doses and producing metastatic calcification of soft tissues; of these, the renal tubules and arterioles and the media of the large blood-vessels are most affected. If the toxic doses are stopped the calcareous deposits are said almost to disappear. The serum calcium and phosphorus tend to be grossly raised, but not always—so that the serum calcium level is not a reliable guide. Serum calcium estimations in 12 of our cases after varying dosage and periods on the drug showed levels of between 10.1 and 10.8 mg. per 100 c.c. in 6 cases; in 3 cases the levels were approximately 11 mg., and in 3 cases there was hypercalcaemia, viz. 12.6, 13.8, and 14.8 mg. per 100 c.c. respectively.

From a review of the clinical results of many workers who have used calciferol in diseases such as chronic arthritis, Bicknell and Prescott (1942) found that most patients tolerated calciferol in doses of from 200,000 to 400,000 i.u. daily. They quote Steck and collaborators as stating, from extensive observations on over seven hundred patients, that few show toxic symptoms unless the dose exceeds 10,000 i.u. daily per pound of body-weight. Bicknell and Prescott, however, think these doses are far too high. From the clinical point of view they conclude (1) that, if large doses must be given it is useless to rely entirely upon blood calcium estimations as a safeguard, the clinical symptoms of poisoning being a better guide; (2) that the giving of highly concentrated vitamin D and calcium preparations together is unwise; (3) that fish liver oils should be the source of high doses of vitamin D; (4) that in patients with nephritis or cardiovascular disease large doses are unwise.

Regarding our patients, there have been symptoms of intolerance in eight of the thirty-eight. However, apart from Dr. Dowling's first case, who said he was severely upset on two occasions, the symptoms have been mild, consisting chiefly of nausea, loss of appetite, depression, or feeling out of sorts. We attributed the nausea mostly to simple irritation of the drug on the gastric mucosa, as it generally was felt soon after ingestion and then passed off. The symptoms have occurred usually in patients taking 150,000 i.u. daily, but the toxic threshold is said to vary considerably.

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 STECK, I. E. *et al.* (1937) Further Studies on Intoxication with Vitamin D, *Ann. Int. Med.*, 10, 951.

Dr. J. E. M. Wigley: I think we are all agreed that the results of this treatment, demonstrated by these six cases, is most striking; one might almost say epoch-making. The lady (Case 11) I saw at Charing Cross Hospital about two years ago when she had a definitely florid type of lupus vulgaris affecting her face. As she lives at Luton, and travelling conditions were very difficult at that time, and she was 70 years of age, I told her that I did not think any more could be done than was being done then. To-day I see her, to all intents and purposes, cured!

I think not the least important aspect of this treatment is an economic one. Treatment of lupus by other methods, e.g. Finsen light, general U.V.L., &c., has always had the great disadvantage of being very costly, both in apparatus and staff required, and in the patient's time, including loss of earning capacity. I do not wish to say that we can now dispense with these methods of treatment, but if the response to calciferol shows the continued, generally excellent results demonstrated to-day, a great advance will have been made in the method of dealing with this very serious social menace.

Dr. P. J. Feeny: I saw Case I several times when he was having Finsen light, and have not seen him again until now, when he is greatly improved.

Dr. R. M. B. MacKenna: There is some evidence that dermatologists in France are working along the same or similar lines and therefore I would urge Dr. Dowling and Dr. Prosser Thomas to publish an account of their work at an early date. I should like warmly to congratulate the exhibitors of these cases on the excellent results which they have achieved.

The President: We all congratulate Dr. Dowling and Dr. Prosser Thomas very sincerely. These cases are absolutely dramatic. I have not seen anything so promising for very many years.

Dr. G. B. Dowling: I have little to add except to thank Dr. Prosser Thomas for all the trouble he has taken in collecting and keeping records of these cases. Those that have been shown to-day have had no treatment whilst under our care except calciferol by mouth, but they are selected cases. As regards the other cases which we have treated with calciferol I think it is fair to say that all of them appear to have improved, but by no means all to the same extent.

Lupus Vulgaris Verrucosus of the Buttocks.—H. CORSI, F.R.C.S.

G. P., male aged 49.

Examination.—On the medial part of the buttocks are symmetrical areas, of a dark red, vegetative state of the skin, each area being rather larger than the size of a hand and fingers. The lesions are abruptly margined, the margins appearing much more active than most of the central area, where some places show spontaneous recovery.

There is a clear area between the medial margin of each lesion and the anal skin. Rectal examination was negative.

There is a patch of lichenification on the left shin, which has been present for twenty years. This has given no trouble except some itching, which, following some X-ray treatment, has now ceased completely.

The Wassermann reaction is negative.

History—statement by patient.—He was never conscious of anything abnormal until the early part of 1945. From 1941 to June 1944 he used to go to business in his car, but after that he took to riding a bicycle. Some six months later, he noticed blood on his underclothing, and found some blood blisters on the inner surface of his buttocks. Excepting for some soreness, the condition gave him no trouble, and was only seen by his general practitioner, Dr. Hector of Letchworth, in June 1945, when the patient was examined on account of lumbago.

He was in the Army in 1939-41, and went to France. He had a fall from a wagon early in 1940, suffering severe bruising of the buttocks. This took several weeks to clear, but the patient says that after some months there was nothing left to see of this bruising. He has always been in good health except for "bronchitis", which troubles him most winters. His mother and brother died of tuberculosis. An X-ray photograph of his chest shows a large cavity in the left upper zone.

Examination of the small quantity of sputum which he was able to produce shows the presence of tubercle bacilli. The E.S.R. rate is 12 mm.

Diagnosis.—Chronic phthisis, probably of many years' standing.

Treatment.—There was improvement following the use of penicillin cream, which was tried in the belief that the condition might be a staphylococcal vegetative condition. There was improvement, also, in two smaller areas treated with X-rays.

Section.—The appearances are typical of lupus vulgaris.

Now that I have seen Dr. Dowling's and Dr. Prosser Thomas's cases I shall certainly put him on calciferol, and I hope I may have an opportunity of bringing him up here again, when we may note the therapeutic result.

Dr. J. E. M. Wigley: Does anyone know of the use of calciferol in tuberculosis in other parts of the body?

Dr. Prosser Thomas: I have not seen any references to its use in concentrated form in tuberculosis elsewhere.

Alton. This was the only case in which we have had an opportunity of trying calciferol in lupus in childhood and in an early stage.

COMMENT

Calciferol (vitamin D₂) is a potentially toxic drug. It is a purely artificial substance, prepared by exposing the vegetable sterol, *ergosterol*, to ultraviolet light. It is said to be almost always contaminated with other possibly toxic by-products of irradiation, and to be more toxic than the naturally occurring vitamin D₃, which is found in animal products such as egg-yolk, butter, and fish liver oils, and is derived from irradiated animal sterols (Bicknell and Prescott, 1942).

Though apparently never tried hitherto in lupus, calciferol has been used in a variety of other diseases, often in very high dosage, and toxic symptoms have been observed not infrequently and reported in the literature. General well-being and a good appetite are said to be often the first symptom of poisoning. Anorexia may follow, together with nausea, vomiting, diarrhoea, and polyuria. Mental depression and headache may be early symptoms. Excessive doses mobilize phosphorus and calcium, thus broadly having an opposite effect to normal doses and producing metastatic calcification of soft tissues; of these, the renal tubules and arterioles and the media of the large blood-vessels are most affected. If the toxic doses are stopped the calcareous deposits are said almost to disappear. The serum calcium and phosphorus tend to be grossly raised, but not always—so that the serum calcium level is not a reliable guide. Serum calcium estimations in 12 of our cases after varying dosage and periods on the drug showed levels of between 10.1 and 10.8 mg. per 100 c.c. in 6 cases; in 3 cases the levels were approximately 11 mg., and in 3 cases there was hypercalcaemia, viz. 12.6, 13.8, and 14.8 mg. per 100 c.c. respectively.

From a review of the clinical results of many workers who have used calciferol in diseases such as chronic arthritis, Bicknell and Prescott (1942) found that most patients tolerated calciferol in doses of from 200,000 to 400,000 i.u. daily. They quote Steck and collaborators as stating, from extensive observations on over seven hundred patients, that few show toxic symptoms unless the dose exceeds 10,000 i.u. daily per pound of body-weight. Bicknell and Prescott, however, think these doses are far too high. From the clinical point of view they conclude (1) that, if large doses must be given it is useless to rely entirely upon blood calcium estimations as a safeguard, the clinical symptoms of poisoning being a better guide; (2) that the giving of highly concentrated vitamin D and calcium preparations together is unwise; (3) that fish liver oils should be the source of high doses of vitamin D; (4) that in patients with nephritis or cardiovascular disease large doses are unwise.

Regarding our patients, there have been symptoms of intolerance in eight of the thirty-eight. However, apart from Dr. Dowling's first case, who said he was severely upset on two occasions, the symptoms have been mild, consisting chiefly of nausea, loss of appetite, depression, or feeling out of sorts. We attributed the nausea mostly to simple irritation of the drug on the gastric mucosa, as it generally was felt soon after ingestion and then passed off. The symptoms have occurred usually in patients taking 150,000 i.u. daily, but the toxic threshold is said to vary considerably.

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Dr. J. E. M. Wigley: I think we are all agreed that the results of this treatment, demonstrated by these six cases, is most striking; one might almost say epoch-making. The lady (Case II) I saw at Charing Cross Hospital about two years ago when she had a definitely florid type of lupus vulgaris affecting her face. As she lives at Luton, and travelling conditions were very difficult at that time, and she was 70 years of age, I told her that I did not think any more could be done than was being done then. To-day I see her, to all intents and purposes, cured!

I think not the least important aspect of this treatment is an economic one. Treatment of lupus by other methods, e.g. Finsen light, general U.V.L., &c., has always had the great disadvantage of being very costly, both in apparatus and staff required, and in the patient's time, including loss of earning capacity. I do not wish to say that we can now dispense with these methods of treatment, but if the response to calciferol shows the continued, generally excellent results demonstrated to-day, a great advance will have been made in the method of dealing with this very serious social menace.

Dermatomyositis.—P. J. FEENY, M.B.

Mrs. A. B., aged 34. *History*.—Admitted seven months ago complaining of increasing weakness in the limbs, backache and for the previous two months a uniform pin-point erythema on the face. For the first month after admission she had a mild pyrexia with increasing wasting of the muscles. Her hair then fell out and the rash spread to the whole body. A dark pigmentation developed on the backs of the hands. The consistency of the muscles became progressively wooden and a pitting œdema developed on the limbs, pressure areas and face.

For the first four months she was treated with vitamins and massage twice a week without improvement; then glycine 5 one t.d.s. and thyroid grain one t.d.s. were substituted for the vitamins. Radiant heat and exercises twice daily were commenced ten weeks ago. From being unable to sit up, to raise her head, arms or legs or to feed herself, she could now sit out of bed, raise her head, raise her arms to shoulder level, raise her feet while in bed to a height of two feet, use a knife and fork and knit and write. The erythema has been fading uniformly for the past month.

Note.—There has been no induration of the skin at any time.

Investigations.—Electrical reactions: (a) Five months ago, all muscles tested responded weakly to strong faradism. (b) Two months ago, in addition there was a strong reaction to faradism in the left forearm, but not in the left leg, and a + + reaction to galvanism in the left leg.

Urine on admission: Albumin and acetone +, culture sterile.

Blood: Meinicke negative. Counts (four examinations), nothing abnormal. B.S.R., 26 Westergren units after one hour; 39 after one and a half hours; 50 after two hours.

X-ray: Shoulder and elbow joints—no evidence of bony changes.

Psychiatric: Suppressed fears with resulting exhaustion. Ego inflation.

Neurological (Dr. Rowland Hill): A polyneuritis plus myositis, probably due to a virus infection. I have recently seen two cases in sisters which developed simultaneously.

Biosis of skin: Sections were shown.

Dr. F. Parkes Weber: I suppose Dr. Feeny does not mean to say that there is hardly any skin factor in the present case of dermatomyositis. Cases of dermatomyositis mostly show œdema at various parts, especially about the eyes, and œdema is doubtless sometimes localized over the affected muscles. In this case, I understand, the patient had decided œdema, as is typical. I think such œdema is really of an active inflammatory nature. I think I am right in saying that as a rule not only is œdema found about the eyes, but that the skin at that part is often reddened and may even be scaly.

Dr. P. J. Feeny: What I had in mind was that the changes developed first in the muscles and not in the skin. There was so much œdema that we could not get into a vein.

Pityriasis Lichenoides with Necrotic Lesions (Habermann).—K. TATZ, M.D. (for L. FORMAN, M.D.).

Male, aged 31. Two attacks of dry pleurisy in 1930 and 1936. His sister had pulmonary tuberculosis. His own affection has been present for two years with new lesions appearing continuously. The condition was diagnosed in the Army as papulonecrotic tuberculide. Blood Wassermann and Kahn are negative, and Mantoux one in 1,000 is slightly positive. X-rays of chest show some thickening of diaphragmatic pleurae. Lesions occur mainly on limbs, buttocks, and upper part of trunk. The penis is affected, and there are two necrotic papules on the left palm. The lesions are as follows: (1) Small macules of waxy appearance on which a fine scale can be seen or produced by scraping; (2) small pinkish-brown papules; (3) larger hæmorrhagic papules, many covered by dark necrotic crusts which separate off to leave superficial ulcers terminating in varioliform scars. Each individual lesion takes about three weeks to develop into a superficial ulcer. The patient complains of slight itching. Treatment for the past six weeks has been weekly injections of 0.05 grammes of myocrisin; the number of new lesions appearing has definitely decreased for the first time in two years.

Points of interest: Involvement of palms, which is unusual; hopeful response to gold therapy; possibility of a tuberculous factor in the ætiology.

Section of a dull-red papule showed in the cutis a dense lymphocytic infiltrate mantling the vessels, some of which are showing multiplication of the cells of the media.

Lupus Vulgaris with Miliary Lymphatic Spread. Epithelioma.—R. P. STRANG, M.R.C.S., L.R.C.P. (for Dr. L. FORMAN).

Male, aged 53, first seen in August 1945. He first noticed a lesion on the back of the neck twenty-six years ago, which has been slowly increasing in size. At no time has he received treatment. Two years ago he noticed a growth on his neck in the centre of the original lesion. Physical examination revealed that the back and left side of the neck was the site of a brownish-red plaque, with atrophic scarring and serpiginous active border. Spreading peripherally over adjoining shoulder was an eruption of satellite papular lesions, lichenoid in character. In the centre of the original lesion was an epithelioma. On the vertex, at site of an old injury, was another area of scarred lupus vulgaris. Red blood count: 5.12 millions; hæmoglobin 100%; white cell count 5,800; sedimentation rate 6 mm. per hour. X-rays of chest normal. Blood Kahn negative. The epithelioma was excised and sections confirmed the diagnosis.

The case is shown because of the epithelioma arising on a plaque of lupus vulgaris that had had no previous treatment with X-rays or light, and because of the peripheral lymphatic spread of satellite lesions.

Dr. A. C. Roxburgh: I do not think it is very rare for an old lupus vulgaris to develop an epithelioma even if it has not had X-ray or light treatment. I remember a Continental paper (G. Truffi, *Arch. ital. Derm.*, 1933, 9, 443) in which it was found that most cases of carcinoma arising on lupus vulgaris occurred in patients who had had neither X-rays nor any other form of therapy. (1935, *Abst. Year Book Derm. Syph.*, Chicago, p. 301.)

Dr. G. B. Dowling: The impression most people have is that the incidence is higher in cases that have been irradiated. Quite a number of years ago it appeared to be agreed among dermatologists that for this reason lupus should not be treated by means of X-rays.

Abnormal Mesodermal Pigmentation.—ALICE CARLETON, M.D.

This is a healthy British girl of 13 with profuse bluish spots on the upper trunk and face, mouth, iris, and sclera. The condition is associated with bossy thickening of the skull, due to ballooning of the bones of the posterior cranial fossa. The spots differ from a blue nevus in their distribution—they are profusely disseminated—and in their histology, which shows no circumscription. They also differ from Mongolian blue spots, which have never been described in fair or red-haired children, and which tend to fade away instead of increasing in number. There is, further, nothing to suggest the presence of the diffuse mesodermal pigmentation associated with melanin excretion in the urine which has been described in animals. One must therefore conclude that this case represents an abnormality in mesodermal pigmentation which has not hitherto been described and which, at any rate in this instance, is associated with a skeletal abnormality, presumably congenital.

Dr. F. Parkes Weber: I suggest that the case may be an atypical pigmentary incomplete form of Recklinghausen's neurofibromatosis, to some extent analogous to that of a girl, aged 14 years, which I described in 1905 (*Brit. J. Derm.*, 1905, 17, 226, and 1909, 21, 49). The disease at that time was practically limited to a good deal of pigmentation of various types, but when examined again in 1926 (*Proc. R. Soc. Med.*, Sect. Derm., 1927, 30, 22) it had become a fully developed one of Recklinghausen's disease. She had been married for some years and had a child; the sprouting of the molluscous fibromata may well have been favoured in some way by the pregnancy and child-birth. What will happen in Dr. Carleton's patient when she grows up? The two cases are, however, not quite alike, and perhaps it would be better not to suggest that in Dr. Carleton's patient the condition is likely specially to be affected by marriage and possible pregnancy.

In a paper with Dr. J. R. Perdrau (*Quart. J. Med.*, 1930, 23, 151) I pointed out that as neurofibromatosis was a manifestation of an inborn abnormality of development, it was not surprising that it should be occasionally associated with other congenital or developmental abnormalities. In Dr. Carleton's patient there is the remarkable abnormality of the shape of the posterior part of the cranium. Moreover, she has definite over-extensibility of the elbow-joints, reminding one of what is seen in some cases of the Ehlers-Danlos syndrome. In this connexion it should be noted that the biopsy scars have a somewhat "atrophic" appearance, reminiscent of scars in patients with "cutis laxa" and the fully developed Ehlers-Danlos syndrome.

Section of Odontology

President—LILIAN LINDSAY, M.D.S.Durham, L.D.S.Ed.

[November 26, 1945]

Reflections on the Development and Present General Application of Acrylic to Conservative Procedures

By ROBERT CUTLER, L.R.C.P.Lond., M.R.C.S., L.D.S.Eng.

THE purely practical exploitation of acrylic, inevitable in the stress and strain of the war years, has had its disadvantages, as this material lends itself so easily to every variety of expert manipulation, so that the essential principles underlying its character and usage have been somewhat neglected. As might have been imagined, the results of enthusiastic and quite empirical technical adventures have often been disastrous, and not made any the less serious by a spate of technical articles and notes advocating "short cuts" in procedure, this avalanche completely drowning the relative trickle of really scientific dental contributions in this specialized subject.

Methyl methacrylate first came into accepted dental use under the trade name "Paladon" in or about 1937, and it was about 1940 that a specialized product, under the trade name "Portex", first became available for purely conservative procedures, experience with which inspired an article by S. A. Leader (1942), so courageously titled "A Dental Revolution".

Very soon, however, in spite of the advantages of the new material, major difficulties arose, such as lack of colour fastness, inexplicable breakage, or detachment of restorations. This necessitated, for those whose faith was still unshaken, a further period of experimentation, review, and research, though, under the war conditions then obtaining, the latter was largely trial-and-error clinical investigation with bench testing under conditions of no real scientific accuracy.

It is interesting to note that lessons from these failures were being closely studied by other groups handling acrylic material, though it was not until 1943-44 that other proprietary brands became available, since when the user has the choice of at least three accredited sources of supply.

Bearing in mind the fact that for conservative procedures a dense homogeneous effect is essential, it can be realized that for this an extremely fine powder base is a prerequisite, and it is noteworthy that the sources of supply differ somewhat in their composition, to the extent that one is essentially of fine primary granule form, and at least one other of a primary coarse granule, secondarily ground into a fine powder base by mechanical means. Advantages are claimed for each, but so far no strictly controlled tests by any independent authority have yet been made available, and here at least is one opportunity for research by those qualified to undertake it.

In general, however, we can regard 1943-44 as the turning point in stabilization of supply, whereby new workers in the field have been spared many unnecessary difficulties, and fresh fields opened to those already possessing greater experience, the net result being that clinical work now undertaken bears, and most certainly merits, the strictest independent investigation.

In its purely general aspect, however, it does seem to me that one most important consideration has been consistently overlooked, and that is, how the paramount advantage of this material lies in the fact that it strictly conforms to the basic substitution principle which has been the foundation of dental technique for the last half century or more, and which separates the dentist's art from all other branches of mechanical precision work, which depend on the micrometer, the slide rule, or the blue print.

The dentist's method is to form the case in wax, to invest, and if necessary reverse it, to dissipate the wax, and to introduce into the cavity so formed his permanent material, whether vulcanite, acrylic, or molten metal, so producing a facsimile replica of his wax conception.

This process is virtually unique, and I cannot think of an exact analogy in any other sphere, and, indeed, we have only to compare the construction of a post crown in gold and china to one fabricated in acrylic, to see how closely the latter conforms to the time-tested principle. With the gold china preparation a post and metallic root-cap have to be prepared and fixed together, a china tooth, or facing purchased from the appropriate agency and subsequently ground to shape, being then joined to the base by cement or solder, so producing a composite result, mechanically sound enough, but only too often completely unæsthetic.

By the new method it is only necessary to fit a post to the canal of the prepared tooth, any non-corroding metal will serve, to build upon it a wax form to the character required,

Dr. R. M. B. MacKenna: It seems to me that these necrotic lesions, very widely scattered and extremely deep, are slower in healing than is usually the case in this particular disease. Also, on examining the patient I cannot see much sign of any lichenoid element. Originally a diagnosis of papulonecrotic tuberculide was made, and to my mind the clinical facts point more to that diagnosis than to the one now stated.

Dr. G. B. Dowling: I would certainly support the present diagnosis of pityriasis lichenoides acuta in this case; the angry-looking nodules with their striking, almost black hæmorrhagic central necrosis are most characteristic.

Dr. Louis Forman: I disagree with Dr. MacKenna although the differential diagnosis between pityriasis lichenoides with necrosis and papulonecrotic tuberculide may be difficult. The early papule did not show any suggestion of a tuberculous histology. Further the hæmorrhagic necrosis involved the whole of the larger papules and not the summit as in a papulonecrotic tuberculide. Flat, lichenoid papules were demonstrated.

Keratoderma Punctata.—CLARA M. WARREN, M.D.

Man of 57; shows typical lesions of keratoderma punctata on palms, fingers and soles. They have been present for only five years, and have slowly increased in number. Crateriform pits with surrounding thickening are the characteristic lesions. The man has worked as a butler until three years ago, and can give no history of contact with arsenic. None of his relatives has had any similar condition. The thickened hard punctæ cause him no trouble except on the finger tips, where pain occurs on pressure.

Dr. Louis Forman: Keratoses of the palms in middle-aged people might well be due to their having taken arsenic some years previously. In Dr. Warren's case there was no history of medicine which might have contained arsenic having been taken for rheumatism, epilepsy or chorea, but there are other possibilities, e.g. arsenic in drinking water, or absorption by inhalation of arsenic liberated by the action of moulds in wall-paper.

Dr. G. B. Dowling: I disagree with Dr. Forman in this case. If the warty lesions were due to arsenic one would expect arsenical changes to be present elsewhere; moreover, this is a not very uncommon picture and very characteristic of one of the late developmental abnormalities.

Dr. A. C. Roxburgh: In such a case would not arsenic be found in the hair or the epidermis?

Dr. Clara M. Warren: Can any treatment be suggested for this case?

Dr. R. M. B. MacKenna: If arsenic has played any part in the ætiology it might be worth while trying BAL (OX 217), a British preparation, the formula for which is secret, but which has the endorsement of the Medical Research Council, and is used for arsenic intoxication.

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It is interesting to note that lessons from these failures were being closely studied by other groups handling acrylic material, though it was not until 1943-44 that other proprietary brands became available, since when the user has the choice of at least three accredited sources of supply.

Bearing in mind the fact that for conservative procedures a dense homogeneous effect is essential, it can be realized that for this an extremely fine powder base is a prerequisite, and it is noteworthy that the sources of supply differ somewhat in their composition, to the extent that one is essentially of fine primary granule form, and at least one other of a primary coarse granule, secondarily ground into a fine powder base by mechanical means. Advantages are claimed for each, but so far no strictly controlled tests by any independent authority have yet been made available, and here at least is one opportunity for research by those qualified to undertake it.

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In its purely general aspect, however, it does seem to me that one most important consideration has been consistently overlooked, and that is, how the paramount advantage of this material lies in the fact that it strictly conforms to the basic substitution principle which has been the foundation of dental technique for the last half century or more, and which separates the dentist's art from all other branches of mechanical precision work, which depend on the micrometer, the slide rule, or the blue print.

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By the new method it is only necessary to fit a post to the canal of the prepared tooth, any non-corroding metal will serve, to build upon it a wax form to the character required,

to make a check test for the appropriate colour and distinctive markings, and thereupon, by the time-tested principle of substitution, produce a perfectly æsthetic restoration, adequate in strength, kind to the tissues and with true finesse of mechanical fit: no laborious soldering, fitting, or grinding or any of the tedious procedures which smack more of the fitter's bench than the vital art of the dental surgeon. This is perhaps an over-simplification and it is freely admitted that composite restorations of cast metal and acrylic have a high place in this specialized field, but it illustrates the point I have in mind with which any student of dental history would surely agree.

A further primary principle can be noted here, if one recalls that before the war soap carving of tooth forms was rightly favoured in some British schools, though inevitably it was regarded as an end in itself in the sense that it was meant to inculcate an appreciation of the æsthetics of form, and the value of manual dexterity generally: beyond that it was impossible to go, as the student could hardly be expected to visualize a transformation of his carving into a mass of gold, china and cement. With the acrylic medium available, however, he can now carve his forms with the added incentive of knowing the results of his labour can be reproduced in a tooth-like solid, losing not one whit of the character which he has so carefully formed. This point should not be neglected by the schools where facilities for experiment and research should be superior to those of the free-lance worker.

I have already referred to the spate of technical articles as being disadvantageous, and we do not lack for specific examples, for as early as 1942 I drew attention (Cutler, 1943) to the fact that test inlays of M.O.D. form, made by the pressure plunger and sprue channel method, were in no way superior, and usually inferior, to those made by the simple "split flask" technique, even when the pressure plunger assembly was made as a precision mechanical unit. At that time the reason was not fully clear to me, but what was abundantly clear was the fact that other workers had noticed the same phenomenon, and in some cases had gone to extravagant lengths in the field of mechanical improvisation in order to justify its continued use: thus one worker advocated an assembly whereby the inlay cavity part was boiled in water whilst an electric cooling fan was made to play on the pressure plunger and reservoir—and further, one manufacturer, not one whit discountenanced by these procedures, did in fact advocate the pressure plunger technique as a standard method.

In this connexion it is interesting to show the value of accurate scientific information, in that it was a fresh study of the classic articles by Tylman (1942*a, b*) that gave us the clue to this apparent anomaly. Tylman had made it very clear that the greatest acrylic mix fluidity range was fairly critical, lying between 70° and 90° C., that the greater part of the polymerization occurred in this period, and that any additional pressure after this point only resulted in additional strain in the processed piece. In such circumstances it would be reasonable to suppose that using the two-part flask method, with the mould filled to excess, there should be a point in the initial curing process, when, as the temperature rose progressively, fairly sudden closure should occur under a constant spring pressure, indicating the phase of maximum fluidity and high rate of contraction, but this had never been a marked feature in our experience.

In considering the whole matter again, however, we realized that in the two-part flask technique the extruded "flash" being subject to greater pressure and certainly greater initial heat, in virtue of its peripheral position, hardened first, thus obstructing closure at the critical period, and that the same premature hardening occurred in the reservoir cylinder of the pressure plunger method. In each case the effect, as far as "follow up" of contraction was concerned, was bad, but obviously would be worse, if not disastrous, in a reservoir and sprue channel system, and this was strictly in accordance with the observations made. To elucidate the matter further, and if possible to confirm Tylman's observations, we developed a closed flask assembly with an excess charge of material located in direct contact with the main mass under control of a pressure pin with screw thread feed, operated from the outside of the sealed and clamped flask assembly, and, as might have been expected, it was found that almost effortless turning of the threaded pressure pin could be effected during one phase of the initial curing period, resistance to turning pressure having been constant both before and after this phase.

In view of these findings certain modifications in the two-part flask processing technique were obviously called for and these were summarized in a further article (Cutler, 1944) and, to my knowledge, the validity of the technique as then formulated has not since been challenged. This whole incident has been quoted at some length in showing the value of accurate scientific information being freely available when difficulties are encountered, as distinct from the employment of mechanical ingenuity to compensate for errors arising from a misconception of the phenomena involved.

At this stage, it might be suggested that the greater wealth of articles of a scientific nature on prosthetic aspects of acrylic manipulation would be of material assistance,

and certainly articles similar to that contributed by Taylor (1941) come within this category, but even so there is some little danger of carrying the analogy too far, as the permissible margin of error in delicate conservative restorations is obviously infinitely less than in relatively massive prosthetic pieces. For example, at first blush the fracture of M.O.D. acrylic inlays, when exposed to negligible occlusal stress, might be considered analogous to the incidence of fracture across the vault of a partial acrylic denture which is not uncommon, but in actual fact, in the latter instance, it is the combination of low resistance to extension (low tensile strength) operating on one surface of the denture and high resistance to compression operating on the other surface that causes cracking and fracture, if by any mischance an over-great bending or squeezing force is applied across the long axis of the vault of the denture.

On the other hand in the acrylic denture of M.O.D. type uncontrolled—and often unnoticed—contraction of the piece, prior to cement fixation under positive pressure, may well produce internal strains of an altogether different character and quality, but none the less leading to spontaneous fracture under negligible load.

Again, because in prosthetic practice the virtually complete unbreakability of acrylic teeth is a known fact, it should not be assumed that every form of acrylic conservative restoration will be equally successful, and, indeed, in gold acrylic composite bridgework spans, very considerable trouble has been experienced, due largely to the present relatively low tensile and sheer strength of the material; a study of progress in composite bridge-work design being especially instructive. In the early days it was considered sufficient to place a plain round bar in the body of the span, later cranked to prevent torsional breakdown of the material, but in many cases a complete fracture of both metal bar and acrylic mass was noted. The next step was a progressive thickening of the reinforcing metal element, which, however, in the end defeated its own object, as the acrylic became a virtually unsupported veneer, the result being a crazing and cracking with eventual complete disintegration.

The problem has now been solved by diffusing a relatively delicate reinforcement throughout the acrylic mass, or by employing a cast metal occlusal surface to which the body of acrylic is fused, and it is interesting to note that our own trends of design find confirmation in a recent article by Salisbury (1945) which, although essentially practical, is one of the most sober and helpful reviews available recently. On the other hand examples can be cited of the value of articles on prosthetic matters, such as the demonstration of internal strain in large dentures made in clear acrylic, either by solvent crazing or by the polariscope, suggesting that similar phenomena may occur in delicate conservative pieces, particularly when one recalls how much greater the applied unit pressure can be, and how easy it is to apply such enhanced pressures at the wrong stage of the time-heat-pressure cycle.

To consider the matter from another angle, the evaluation of the suitability of acrylic by response to simple mechanical testing has sometimes led us astray, as, for instance, the initial acceptance of Brinell hardness as a criterion of wear resistance. (Examples B.H.T. acrylic 26-35, 24 ct. gold 29, 22 ct. gold 54, amalgam 80-100.) On this scale doubts were expressed as to the wear resistance of acrylic, but the fact seems to be the inherent resilience factor, and the presence of saliva as a lubricant confers a quite unexpectedly high resistance to abrasion. The plastics engineer would, however, be not so greatly surprised, as he would bear in mind the performance of laminated plastic bearings and gear wheels in standard industrial practice. For instance, it has been found that plastics employed for the master bearings in steel roller mills have a life four times as long as phosphor-bronze bearings, the coolant lubricant being water, thus having a most interesting analogy to the saliva performing the same function in the mouth: further, in gear drive practice when the load and drive were irregular the shock-resisting quality inherent in the plastic gear train invariably produced a more even and more smooth transmission. ("Plastes" 1943.)

Peyton and Mann in a masterly contribution (1942) seemed well aware of this phenomenon and considered the Bierbaum scratch test as a better indication of wear-resisting properties, and worked out a "scratch resistance number" for a series of materials which seem more in accord with clinical behaviour. (Examples S.R.T. acrylic 49-61, 24 ct. gold 44, 22 ct. gold 71, amalgam 150.) It would appear the resilience factor is of significance here, but this property, from our standpoint, is a rather two-edged sword, as, whilst the shock-resistant quality apparently aids its resistance to abrasion, it is equally clear that the consequent lack of rigidity would be, and is, a positive danger in thin section, or unsupported, acrylic restorations, so that with material at present available the incisal stress, and we can only assume that the support inherent in a good jacket crown preparation, in which no part of the restoration is exposed to leverage or flexural

to make a check test for the appropriate colour and distinctive markings, and thereupon, by the time-tested principle of substitution, produce a perfectly æsthetic restoration, adequate in strength, kind to the tissues and with true finesse of mechanical fit: no laborious soldering, fitting, or grinding or any of the tedious procedures which smack more of the fitter's bench than the vital art of the dental surgeon. This is perhaps an over-simplification and it is freely admitted that composite restorations of cast metal and acrylic have a high place in this specialized field, but it illustrates the point I have in mind with which any student of dental history would surely agree.

A further primary principle can be noted here, if one recalls that before the war soap carving of tooth forms was rightly favoured in some British schools, though inevitably it was regarded as an end in itself in the sense that it was meant to inculcate an appreciation of the æsthetics of form, and the value of manual dexterity generally: beyond that it was impossible, to go, as the student could hardly be expected to visualize a transformation of his carving into a mass of gold, china and cement. With the acrylic medium available, however, he can now carve his forms with the added incentive of knowing the results of his labour can be reproduced in a tooth-like solid, losing not one whit of the character which he has so carefully formed. This point should not be neglected by the schools where facilities for experiment and research should be superior to those of the free-lance worker.

I have already referred to the spate of technical articles as being disadvantageous, and we do not lack for specific examples, for as early as 1942 I drew attention (Cutler, 1943) to the fact that test inlays of M.O.D. form, made by the pressure plunger and sprue channel method, were in no way superior, and usually inferior, to those made by the simple "split flask" technique, even when the pressure plunger assembly was made as a precision mechanical unit. At that time the reason was not fully clear to me, but what was abundantly clear was the fact that other workers had noticed the same phenomenon, and in some cases had gone to extravagant lengths in the field of mechanical improvisation in order to justify its continued use: thus one worker advocated an assembly whereby the inlay cavity part was boiled in water whilst an electric cooling fan was made to play on the pressure plunger and reservoir—and further, one manufacturer, not one whit discountenanced by these procedures, did in fact advocate the pressure plunger technique as a standard method.

In this connexion it is interesting to show the value of accurate scientific information, in that it was a fresh study of the classic articles by Tylman (1942*a*, *b*) that gave us the clue to this apparent anomaly. Tylman had made it very clear that the greatest acrylic mix fluidity range was fairly critical, lying between 70° and 90° C., that the greater part of the polymerization occurred in this period, and that any additional pressure after this point only resulted in additional strain in the processed piece. In such circumstances it would be reasonable to suppose that using the two-part flask method, with the mould filled to excess, there should be a point in the initial curing process, when, as the temperature rose progressively, fairly sudden closure should occur under a constant spring pressure, indicating the phase of maximum fluidity and high rate of contraction, but this had never been a marked feature in our experience.

In considering the whole matter again, however, we realized that in the two-part flask technique the extruded "flash" being subject to greater pressure and certainly greater initial heat, in virtue of its peripheral position, hardened first, thus obstructing closure at the critical period, and that the same premature hardening occurred in the reservoir cylinder of the pressure plunger method. In each case the effect, as far as "follow up" of contraction was concerned, was bad, but obviously would be worse, if not disastrous, in a reservoir and sprue channel system, and this was strictly in accordance with the observations made. To elucidate the matter further, and if possible to confirm Tylman's observations, we developed a closed flask assembly with an excess charge of material located in direct contact with the main mass under control of a pressure pin with screw thread feed, operated from the outside of the sealed and clamped flask assembly, and, as might have been expected, it was found that almost effortless turning of the threaded pressure pin could be effected during one phase of the initial curing period, resistance to turning pressure having been constant both before and after this phase.

In view of these findings certain modifications in the two-part flask processing technique were obviously called for and these were summarized in a further article (Cutler, 1944) and, to my knowledge, the validity of the technique as then formulated has not since been challenged. This whole incident has been quoted at some length in showing the value of accurate scientific information being freely available when difficulties are encountered, as distinct from the employment of mechanical ingenuity to compensate for errors arising from a misconception of the phenomena involved.

At this stage, it might be suggested that the greater wealth of articles of a scientific nature on prosthetic aspects of acrylic manipulation would be of material assistance,

Section of Surgery

President—ERNEST FINCH, M.D., M.S., F.R.C.S.

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DISCUSSION ON SURGERY OF THE PATENT DUCTUS ARTERIOSUS

(INFECTED AND UNINFECTED)

Mr. John B. Hunter: For many years the branch of congenital heart disease associated with a patent ductus arteriosus has been the subject of much discussion. Many of these discussions have been academic and have been associated with explanations to account for the closure of the ductus, none of which is really satisfactory.

Barclay, Bancroft and others from the experimental side, using radiological methods in sheep fetuses, have demonstrated that blood ceases to flow through the ductus within a few minutes of birth; but this does not necessarily mean that the ductus is completely occluded as rapidly as would appear from the radiological findings. The ductus is a thick muscular tube at this time and it is possible that with the filling of the whole pulmonary system with the first breath, the flow of blood through the ductus ceases and that vessel, as is common with all vessels denuded of blood in their interior, immediately contracts, and after its occlusion, fibrosis takes place producing the ligamentum arteriosus. This may be over-simplification of the problem but it is one to which I will refer later in connexion with the persistent patent ductus and the flow of blood in it.

The problems associated with a patent ductus arteriosus have had fresh light thrown on them by the intervention of the surgeon in this field, and to some extent theoretical views have been replaced and in the course of time most of the problems will be solved.

Ligation of the patent ductus arteriosus was first suggested by Munroe in 1907 and the first attempt was made by Graybril and Strieder in 1938, but this was not successful. The first successful cases were reported by Gross in 1939 and his approach is now generally used with modifications in the technique. All authorities agree that the patent ductus carries a definite morbidity but it is extremely difficult to assess, and, further, it has not been possible to say accurately to what extent it shortens life, but that patients with a patent ductus do not attain old age is generally agreed, although Gilchrist has reported a case of spontaneous closure in a child.

The chief danger is infection causing a subacute endocarditis which is fatal, but it is to be remembered that these patients, apart from the infective danger, have to live the restricted life associated with a cardiac lesion. The diagnosis of the condition is not always an easy one, and this is not the place to enter into such a discussion, it being in the realm of the cardiologist. There are, however, some cardinal points in the uncomplicated case that may be mentioned. The patients usually are known to have had a cardiac lesion from childhood. They are usually small in size and they may complain of shortness of breath, but usually as they have had the lesion all their life, they are not conscious of this disability. On examination they have no finger clubbing and usually no cyanosis. Palpation over the pericardium may or may not reveal a turbulent heart action, and a thrill over the upper part of the left chest, its maximum about the second interspace. Auscultation reveals the characteristic murmur suggesting a heavy machine shop and known as the "machinery murmur"; its essential feature, originally described by Gibson, is its continuous quality.

An X-ray of the chest usually reveals certain characteristic features, the pulmonary artery is enlarged so that a bulge can be seen below the aortic knuckle and there is usually some enlargement of the heart. The vascular shadows in the lungs are very obvious and in some cases markedly so.

My experience has been chiefly with uninfected cases, only two out of fifteen cases suffered from bacterial endocarditis.

In consultation with Dr. East, who has seen all the cases with me, a decision has been made as to whether operation should be undertaken or not. We have decided that the mechanical defect, together with the risk to life, is sufficient to warrant surgical intervention, in the uncomplicated case, with the exception of the very young; the parents of these children being told to bring the child up at a later date with a view to operation. In the majority of cases a search for septic foci is made; usually, owing to the cardiac condition patients have not had their tonsils and adenoids removed and, where necessary, this is now a routine, the operation being performed under prophylactic doses of the sulpha drugs. Breathing exercises are instituted as soon as the patients come into hospital and are continued throughout their stay. The operative technique has been

stress, allows only the good qualities of the shock-resistant material to be made manifest.

Again, the question of change, both linear and volumetric, due to water imbibition, is clearly of significance, and though at first lack of cementation adhesion was attributed to this sole cause, clinical evidence indicates this assumption is not wholly true, though it is obvious that time be allowed for full water absorption by the processed piece prior to surface drying and cementation.

Tylman (1942a) assumed the original net processing shrinkage of 0.5% approx. was more than compensated by what he called the "available total water expansion" of 0.8 to 1.0%, thus leaving a plus final dimensional change, and this he repeated in a later communication (Tylman, 1942b), but Peyton and Mann (1942), as a result of tests on one-inch lengths of one-quarter-inch square section acrylic specimens, although confirming there was a linear shrinkage of 0.2 to 0.5%, becoming maximal after drying for a month in air at room temperature, said that the linear expansion after prolonged immersion in water was only of the order of 0.02%, thus leaving a total shrinkage discrepancy of 0.48% maximum, which, taken by itself, would suggest the need for a coating investment expanding within such limits. Peyton and Mann, however, did admit their figures had been challenged, and that linear measurements after processing could be invalidated by the tendency of the material to stick to the moulds, and further they admitted that correct closure technique with excess could, in practice, be made to compensate for the initial shrinkage discrepancy.

The salient clinical fact that remains, however, is that in all the jacket crowns made by the author since 1941 only one showed evidence of loosening as far as it was possible to check on regular patients, and, further, that all the jacket crowns that subsequently had to be remade (owing to the use of non-colour-fast material prior to October 1942) needed complete slitting to the root stump, and crosswise leverage in the slit to break them open before they could be removed, so that due precautions being observed, it seems unlikely that water sorption is of too great significance in connexion with cementation, adhesion. What does remain, however, is the undoubted fact of volume change in drying, and it is conceivable that an anterior crown or inlay in a mouth breather might well be susceptible to such changes with fatal results to the fixation of the restoration, and research on this point is obviously indicated. To summarize progress, therefore: (1) The use of colour-fast dyes and stable opacifiers of the native clear acrylic seems established, judging by experience with material available since 1942-43. (2) Improvement in preparation of the basic powders has facilitated the production of a dense homogeneous body mass which is so essential. (3) Knowledge of temperature control, and of the mischievous potentialities of the exothermic reaction, is more widespread, so that porosity, and, equally important, lack of density, in the processed piece, can be regarded as a wholly avoidable evil. (4) Knowledge of control of contraction has advanced to a point where the physical shortcomings of any given restoration can be estimated in advance, and steps taken to compensate for it. (5) The primary supposition of high wear resistance has been amply confirmed in study of clinical behaviour of specimens after three to five years. (6) Design and planning of reinforcement is becoming stabilized judged by the general consensus of opinion of experienced clinical workers.

As regards the direction in which we should look for improvement or help, the following suggest themselves: (1) Investigation of effect of "fillers" of a siliceous nature to increase hardness. (2) Further knowledge of the time-heat-pressure cycle in respect of control of contraction in any given case. (3) Investigation into the effects of monomer showing less shrinkage, and the use of co-polymers of methyl methacrylate itself. (4) Further study of water sorption changes. (5) Strict comparisons of existing materials in tensile impact and sheer strengths either in the pure form, or with specified reinforcement.

This paper is not to be regarded as a scientific study, but as a memorandum of observations based upon a practical empirical study of the material for five years. My own belief is that it has earned its place in our technical armamentarium, and that every scientific effort should be made to investigate all aspects of the use of the material.

Already the names of many workers in this field do not lack for distinction—Leader, Tylman, Peyton, Mann, Salisbury and others—whilst in the related field of acrylic prosthesis we think of Sweeney, Paffenbarger, Taylor, Osborne and so on, and it is to be hoped that the efforts of other distinguished workers will soon be directed to this subject.

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sweeping past the opening acts like a Sprengel's pump. It might be claimed that an artery helps to maintain its lumen full by contracture and this is undoubtedly so, but at this point the aortic wall has a defect, the ductus opening, and, further, the wall is anchored, again by the ductus, so that contraction at this point is not so complete as it is elsewhere in the vessel.

Further evidence of this view is to be found in the remarkable change that takes place after tying the ductus in infected cases. Here shortly after ligation the number of colonies of organisms that can be grown from the peripheral stream is reduced in a most dramatic manner. This can be explained by the fact that the infected blood passing over the vegetations in the pulmonary artery passed before ligation directly into the arterial circulation but after ligation passes into the pulmonary capillary bed where the organisms are presumably destroyed. I have attempted to explain some of the problems presented to us, but both views may be right: it is possible that with the heart acting quietly and the patient at rest, the flow may be from the pulmonary artery to the aorta, then with activity and the heart more vigorously engaged, the pressure in the aorta rises, thus forcing the blood back through the ductus. Such an explanation would account for the slight enlargement of the heart, and the increase in the pulmonary vessel shadows.

On the surgical side, it has been reported from time to time that the murmur has returned after operation; this would suggest the ductus has opened again after being tied. Two experiences of my own can be given in this connexion. In the first the case was an adult with gross infection who eventually died, the murmur having returned about a week after operation. At post-mortem the ligatures were in situ but a thin probe could be passed along the ductus. In this case I think the ductus itself was full of vegetations and that when the ligatures were tied the lumen was occluded, but liquefaction of the vegetations took place, allowing a small channel to appear. The second case was a boy with a very short broad ductus. I tied my first ligature with apparent occlusion, but when I tied my second I found that the first was quite slack, I removed it and replaced it. If I had only put on one ligature I think the murmur might have returned.

Surgeons are not happy about ligation in continuity, and there is no doubt that the next forward step in this region is to divide the ductus completely. I so far have not had sufficient courage to do this, but it is now being done with increasing frequency by others. Crafoord in a personal communication tells me that he always divides the short ones, and ties the long ones, in the latter case injecting a sclerosing fluid between the ligatures. Gross has been wrapping cellophane round the ductus after ligation and this substance causes an intense local reaction.

The difficulties to be encountered during the operation are:— the problems in connexion with exposure, local bleeding of a slight character but sufficient to obscure the field and make the procedure tedious, puncture of the pericardial extension along the ductus with a small constant stream of pericardial fluid, the presence of glands in the arch of the aorta which are sometimes difficult to clear from the ductus, and the most serious, the tearing of the ductus either while it is being defined or due to the ligature material cutting through it. In one of my cases I think the ductus was torn, but fortunately after I had the ligatures round it and was able to secure it.

The complications after operation are on the thoracic side, that is, the patient may get a little fluid or air or both in the pleural cavity. In no case has there been cause for anxiety during convalescence, and by expanding the lung with positive pressure to reduce the air in the cavity there should be no dangers from this side. In an uncomplicated case there should be no blood in the pleural cavity.

The usual convalescence is quiet in children; they are well after twenty-four hours, and it is probably only conservatism that confines them to bed for a week or ten days. One case I must mention, as this is a blot on the series of uncomplicated cases. The child had her ductus ligatured and was getting up when on the tenth day she developed a temperature, a blood culture showed an infection with *Staphylococcus aureus*; there were no mediastinal or chest signs. Penicillin was not readily obtainable at that time and she was transferred to the experimental penicillin unit at the Middlesex Hospital. After a course of penicillin her temperature fell only to rise again in a few days and on this occasion the staphylococcus was found to be penicillin-resistant, and the patient eventually died. I think in this case the operation was undertaken too soon after the child's adenoids were removed, a period of twenty-one days.

I have only operated on two infected cases, both of whom died subsequently. I did not find the operation any more difficult because of the infection. In one case, however, the patient had convulsions during the operation and it is possible that these were due to multiple emboli displaced by manipulation; this was the same case in which the murmur returned after ligation.

the same in all cases and the approach used was that originally described by Gross, although the approach is a limited one, much more so than the chest surgeon usually employs, but it allows the reconstitution of the chest wall more completely and permits, in my opinion, the re-expansion of the lung more easily than the usual thoracotomy incision, although it does not allow the same access in dealing with complications of the operation if one is so unfortunate as to meet them. The patient is placed on his back on the operating table with a small sandbag under the left shoulder, the arm extended above the head; this allows a slightly lateral approach to the mediastinum. A curved incision is made downwards from the sternum opposite the second interspace to the axilla. This incision allows better healing than the straight one. The skin flap is turned up, the pectoralis major incised in the line of its fibres up towards the axilla, the pectoralis minor fibres being divided. The second costal cartilage is divided obliquely close to the sternum, the internal mammary artery is usually not interfered with, but if injured it is divided and ligatured. The pleural space is opened in the second interspace and a single rib spreader introduced, the lung collapses away from the field of operation after the pleura is opened and is lightly packed off with a gauze roll. It is uncommon to find adhesions between the lung and the mediastinal pleura, but if found they are gently separated.

The mediastinal pleura is divided about an inch below the phrenic nerve, which is a noticeable landmark. It is my practice then to clear the lower mediastinal surface of the pleura; this allows certain small veins to fall away into the lax tissue causing no further trouble, or, if they have to be dealt with, they are easily ligated. This blunt dissection also discloses the vagus nerve in the region where the recurrent nerve is coming off, and this latter nerve can be seen winding tightly round the aorta and running more from left to right than is usually realized. This landmark indicates the upper and posterior part of the ductus and by dissection down to the pulmonary artery the lower and left edge of the ductus is defined. The anterior and right edge are more difficult; at first sight there appears to be no space between the arch of the aorta and the pulmonary artery, but by gentle dissection a space is determined and the ductus defined. The posterior surface has now to be freed and it is here that the ductus may be torn; great care, therefore, has to be taken to separate it from the bronchus. The ductus itself when defined is very short and runs more antero-posteriorly than one expects. It can be elongated by gentle traction with a finger on the pulmonary artery while the ligatures are being passed. My custom is to use No. 8 silk and to tie two ligatures, and care should be taken not to damage the recurrent nerve with the ligatures.

The mediastinal pleura is then sutured and the lung expanded by positive pressure. The cut surfaces of the costal cartilage are approximated with a catgut suture, after which the intercostal space is closed. Care should be taken in the closure of the rest of the wound as it tends to heal with an unsightly scar, but since the use of the curved skin incision this is not noticeable. During that period of the operation before tying the ductus the operator is conscious of a thrill, in some cases it is so marked as to be transmitted to the dissecting instruments. This thrill is easily stopped by a finger on the ductus, and it is remarkable what slight pressure is necessary to obliterate the channel; it does not give the impression that one is dealing with arterial pressure. The wall of the ductus itself varies very considerably in thickness. In the majority of cases it is very thin, and in two instances I have been able to see blood moving in the vessel. In both these cases I have had the impression that the flow was from the pulmonary artery to the aorta. This is against all the views previously expressed, but those views have been largely theoretical. It has always been assumed that the flow was from the aorta to the pulmonary artery on the grounds that the pressure in the aorta was more than in the pulmonary artery and also that the enlargement of the heart suggested an extra load in the pulmonary side, this is further strengthened by the increased pulmonary vessel shadows as seen by X-rays. It has been estimated that the flow through the ductus is very large, up to 50% or more of the left ventricular output. It is remarkable that this extra work does not result in more serious signs of myocardial insufficiency, and when the increase in blood-pressure and the great increase in size of the heart that occurs with an arteriovenous fistula of similar size caused by injury is considered, one must ask if there is not some factor present in the congenital case that has not yet been explained.

I believe that the greater part of the flow is from the pulmonary artery to the aorta. It is a little difficult to understand why when the *fœtal* circulation ceases the blood-stream should suddenly reverse, and I think the chief factor is to be looked for in the position of the ductus in relation to the aorta; the opening is placed at the extreme point of the concavity and the high pressure current of blood in the aorta sweeps to the convexity, thus leaving an eddy at the opening of the ductus; further, the blood

Crafoord *et al.* (1944) stated that the absence of the diastolic fraction was incompatible with the diagnosis. It therefore seemed certain that no diastolic murmur meant no patency of the ductus. The accuracy with which the diagnosis could be made was shown by the fact that Shapiro and Keys (1943) found that only two errors had been made in 140 recorded cases submitted to operation. The only certain method of establishing the presence of complicating infection was by blood culture which should be done by the "shake method", but Gilchrist (1945) had pointed out that chest radiography might be of value in demonstrating pulmonary infarcts which only occur in the presence of infection.

The only certain method of establishing the presence of complicating infection was by blood culture which should be done by the "shake method," but Gilchrist (1945) had pointed out that chest radiography might be of value in demonstrating pulmonary infarcts which only occur in the presence of infection.

The indications for surgical closure of the ductus required careful consideration. Infection was undoubtedly an absolute and urgent indication for operation as the prognosis in unoperated infected cases had been almost universally fatal in the past, whereas about 60% (in his own series 7 out of 12) were cured of their infection by closure of the ductus. The severity of the infective process varied from case to case but all patients went progressively downhill so that, when infection had occurred, it was important that its presence should be recognized early and operation undertaken before the patient's general condition had deteriorated. The dogmatism with which one could recommend surgical treatment for cases suffering from superimposed infection had perhaps been slightly diminished by the introduction of penicillin in the treatment of other forms of penicillin-sensitive bacterial endocarditis, for a large proportion of such cases had their blood-stream sterilized and some were apparently cured by prolonged penicillin therapy. However, the results of closure of the ductus had been sufficiently good to make it unjustifiable to use penicillin alone until the drug had been shown to give equally good or better results in cases of valvular infection and this had not been done yet. The speaker had used penicillin on two patients—a boy of 9 in whom penicillin therapy had been started before admission and a girl of 15 who was gravely ill. The boy received a twenty-eight day course of 120,000 units a day which did not prevent his steady deterioration and he died on the table at subsequent operation. The girl also failed to respond after twelve days of treatment and surgery was undertaken as an emergency as a fatal outcome seemed imminent: this child survived operation and had remained free from her infection for six months although she was still seriously ill from a chronic serous pericardial effusion of unknown cause.

Symptoms or signs of cardiac failure were regarded as indications for operation. In addition, enlargement of the heart or a diastolic pressure below 60 were thought to foreshadow failure at a later date and were therefore grounds for surgical treatment. Retarded development in childhood was likewise an indication.

Finally the question arose as to whether the indications should be enlarged to include all cases. The speaker had felt that the wisest approach was to select those with more definite indications until the operation had been shown to carry a low operative risk but he thought that this had now been done and that Mr. Hunter's series confirmed this. He was therefore now of the opinion that all cases should be closed surgically at about the age of 7. If this were accepted, it was essential that the operation should be done only by those who had studied the problem thoroughly, otherwise there would be some terrible tragedies in apparently fit children.

Preparation for operation in the uncomplicated case was not thought necessary. If infection was present a sulphonamide was given for five days before operation in order to reduce the fever: if it failed to do so, penicillin might be tried for a similar period and with the same object.

An intravenous "drip" was started before operation in case of severe accidental hæmorrhage but this was discontinued as soon as the operation was completed as the burden on the heart would be augmented by the infusion of fluids in the absence of blood loss.

An anterior approach through the second intercostal space had been used in the first 17 cases. In the last case (18) a postero-lateral thoracotomy through the fourth space had been employed in order to compare the two methods; in the speaker's view the latter method definitely gave wider exposure and much more room for manipulation and he proposed using it in all subsequent cases.

With regard to isolation of the ductus, it was important to recognize a finger-like process of serous pericardium which often overlapped the anterior part of the pulmonary end of the ductus: this process should not be opened but should be stripped off the ductus towards the heart by blunt dissection: if opened, the constant leak of pericardial fluid obscured the field. Patience and gentleness were the passwords to success in the

Fifteen patients in all have been operated on, two infected—both female—neither of whom recovered, and 13 non-infected, 9 females and 4 males; these made an uninterrupted recovery with the exception of one female whose case is detailed above, who died of infective endocarditis.

The follow-up shows that both the adults and children are more robust and in better general health than before. It would be fair to say that they were unaware until after the ligation of the ductus what limitations had been imposed on them because of their disability. We shall not for many years know the ultimate fate of these patients; we can only say that by ligating the ductus we have reduced their chances of getting a bacterial endocarditis.

Mr. O. S. Tubbs said that Mr. Hunter's series of cases exemplified the much better results obtainable by treating these patients before complications had arisen. In his own 18 cases treated surgically, infection had been present in 12, early heart failure in 3, retarded development in 2, and absence of secondary effects in only 1. The results of treatment in the infected cases compared unfavourably with the uninfected series presented by Mr. Hunter.

He thought that Mr. Hunter's novel suggestion that the blood flow in a patent ductus during post-natal life was from the pulmonary artery into the aorta could not be maintained although it provided a ready explanation for the surprising cure when infection was present. There appeared to be ample evidence in support of the classical view that the blood flow was from the aorta into the pulmonary artery, e.g. (1) in uncomplicated cases there was no cyanosis which would be present if venous blood were sucked into the aorta from the pulmonary artery; (2) the low diastolic pressure usually associated with patency of the ductus was readily explained by the classical view but very difficult to understand if the blood flow were in the reverse direction. He had in fact regarded the diastolic pressure as inversely proportionate to the calibre of the ductus; (3) pulmonary congestion due to the overloading of the pulmonary circulation from the aorta was often found several years before other signs of heart failure developed; (4) dilatation of the pulmonary artery, sometimes with actual aneurysm formation (an X-ray film depicting such an aneurysm was shown), was commonly present due to the raised pressure caused by the flow from the aorta; (5) the oxygen content of blood removed from the pulmonary artery at operation had been shown by Eppinger and Burwell (1940) to be abnormally high; (6) pulmonary infarction always preceded systemic embolism when subacute endarteritis had complicated the picture; and (7) the irrefutable evidence of cardioangiography whereby Steinberg *et al.* (1943) had shown that none of the relatively concentrated dye in the pulmonary artery was seen to enter the aorta.

In reference to the symptoms of persistent patency of the ductus arteriosus, the speaker agreed that retarded development had been overstressed, for 20 out of 23 patients with a patent ductus whom he had seen during the last six years were of average development. Shapiro and Keys (1943) had also noted that only 1 of their series of 23 had appeared underdeveloped.

Symptoms due to heart failure were uncommon before adult life and occurred more frequently where the calibre of the ductus was large, i.e. in cases with a very low diastolic pressure. Breathlessness and orthopnoea often preceded other symptoms of congestive failure owing to the overloading of the pulmonary circulation. X-ray films of the chest of a girl of 15 with gross enlargement of the heart and congestion of the lung fields were shown and followed by similar pictures taken eight weeks after the operation in which the congestion of the lung fields was no longer seen and the heart shadow had diminished considerably in size.

Bacterial infection, causing fever and, sooner or later, pleuritic pain, might arise at any time and without regard to the calibre of the ductus. It was, however, said to be rare before puberty and have its maximum incidence between 16 and 25, but 2 of his 12 infected cases were aged 9 and 10 respectively so that it was clear that too much reliance should not be placed on youthfulness as a protection against infection. The incidence of infection was difficult to determine as most of the available statistics were based on autopsy findings, but it was probably in the region of 30%. Dental extraction had been the precipitating cause of the infection in two of his patients; it was therefore most unwise to consider dental extraction as a minor procedure in a patient with a patent ductus: if the removal of a tooth were essential it should always be accompanied by sulphonamide therapy.

He wished to emphasize that the work should only be done in co-operation with a cardiologist. Dr. Geoffrey Bourne had been his adviser in all cases.

Maude Abbott (1926) had stated that the diastolic fraction of the characteristic murmur might be absent in children but he had never seen such a case, and Hubbard (1944) and

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[December 5, 1945]

Acute Rheumatism in Military History

By J. ALISON GLOVER, C.B.E., M.D., F.R.C.P.

ACUTE rheumatism influences war and preparations for it in five main ways:

(1) It is the cause of a proportion of medical casualties in armies in the field, requiring prolonged treatment.

(2) By its incidence in the form of post-tonsillitis barrack epidemics it may disturb training, and ruin for active service previously healthy recruits.

(3) It is the cause of invalidings from the Services and of pension claims, by reason of consequent heart disabilities.

(4) By causing organic heart disease in children it diminishes the pools of man and woman power for recruiting.

(5) It may be the precursor of more chronic forms of rheumatic disease, to which armies in the field are particularly prone, especially fibrositis, lumbago and sciatica.

It is peculiarly fitting to the theme of this paper that it was the great Thomas Sydenham, a "Puritan captain of horse" "a trooper turned physician" as his few detractors called him, who, in 1683, distinguished acute rheumatism from gout and separated the acute from the chronic forms. Nineteen years before this (1664) De la Martinière had described gonorrhœal rheumatism, a disease which has accounted for some of the so-called acute rheumatism in the earlier estimates, for up to 1860 and later the military attack rates of venereal disease were often incredibly high.

I. ACUTE RHEUMATISM AS A CAUSE OF MEDICAL CASUALTIES IN CAMPAIGNS

The epidemiology of rheumatic fever has long suggested its specifically infectious nature, and, in view of its age incidence, and the fact that its onset is traditionally favoured by damp, exposure, wet clothing and privation, it would seem likely to be prominent among those diseases, which dog the train of war, and which so often take a toll of armies in the field far greater than do wounds or death in battle.

rest of the process of isolation. Like Mr. Hunter, he felt that most reports were too generous in estimating the length of the ductus and he had seen several autopsy specimens in which there was almost no length at all. He had met one such "window-type" of ductus in a child of 9—an uninfected case—and, in the attempt to find a way round, considerable hæmorrhage, probably from the back of the pulmonary artery, had occurred. Fortunately the bleeding stopped spontaneously but it was thought wise to make no further efforts to complete the operation and the child was returned to the ward without the object of the operation being achieved. No ill-effects ensued.

The means whereby permanent closure of the ductus might be invariably obtained was the most outstanding problem of all. Out of 12 patients who were now well following ligation 3 (2 infected cases and 1 with heart failure and a duct of the largest calibre he had yet seen) subsequently had a recurrence of a diastolic murmur which indicated a leak. In spite of complete relief from the symptoms and signs of failure in the one and the cure of the infection in the two infected cases it was begging the point to say that the diastolic murmur was of no consequence for these patients were almost certainly still candidates for infection or reinfection. In view of Gross' (1944) report of 14 consecutive successful cases treated by division between clamps and a further 12 successful divisions by Crafoord *et al.* (1944), this ideal should become the aim in many, if not all, cases.

Closure of the ductus always resulted in an immediate rise of diastolic pressure if this were abnormally low. Frequently the diastolic pressure rose further during the first twenty-four hours after operation without a corresponding rise in the systolic pressure so that the pulse pressure was decreased and the pulse felt "thin," but final adjustment to a normal figure usually followed before the patient left hospital.

The effect of successful ligation in infected cases was most dramatic for the fever immediately abated, although occasionally pulmonary emboli causing sudden transient fever occurred during the first two weeks. The blood became almost or completely sterile within a matter of minutes. The reason for these changes was not yet known.

In conclusion the speaker stated that the results might appear gloomy at first sight but he found encouragement in the fact that there had been no death amongst his uninfected cases and that 7 of the infected patients, who in the absence of operation would now be dead, were still alive.

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Dr. A. E. Barclay presented a short account of some of the researches that he and his colleagues at the Nuffield Institute for Medical Research, Oxford, had carried out on the foetal circulation, in so far as these related to the ductus arteriosus. In some of this work they had had the collaboration of Sir Joseph Barcroft and Dr. D. H. Barron of Cambridge. Sheep, close to full term, were used, the foetus being delivered by Caesarean section. For the initial stage of each experiment foetal conditions were maintained as closely as possible; a nose-bag containing amniotic fluid was applied over the muzzle of the foetus, and the utmost pains were taken to avoid any obstruction to the placental flow through the umbilical cord. For subsequent stages the nose-bag was removed and the umbilical cord divided between ligatures. For the study of the ductus arteriosus radio-opaque media were injected into the external jugular vein, and records of the flow of these materials through the heart and great vessels were obtained by means of cineradiography. The technique was very complex, nevertheless records of the circulation were obtained in some instances within half a minute of delivery. The times of all procedures, including the cineradiographic records, were recorded on a smoke drum.

Dr. Barclay showed lantern slides taken from some of the cineradiographic records, illustrating in the same animal the course of flow from the superior vena cava under foetal and post-natal conditions respectively, i.e. with the ductus arteriosus patent and functionally closed. In healthy animals functional closure of the ductus took place within a few minutes of removal of the nose-bag and ligation of the umbilical cord. If the condition of the animal deteriorated there was a tendency for the ductus to reopen. Post-mortem observations were found to be quite unreliable as to the conditions obtaining in life. In the sheep foetus the ductus arteriosus is large, its calibre approximating to that of the aorta. The flow through the ductus was consistently from the pulmonary trunk to the aorta; there was no indication of any tendency to a flow in the reverse direction. In the experimental records functional closure of the ductus arteriosus took place after functional closure of the foramen ovale.

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But this is not the case. Its role is a much more modest one. It finds no place in Hurst's *Diseases of War* and the various *Bulletins of War Medicine* make hardly a reference.

Even when the disease was far more common and severe in civil practice than it is to-day, its incidence in armies in the field was much below expectation. Thus in the American Civil War of 1861-4 [3c] we find: "The war records, compared with those of our Army before and since the war, do not show any increased prevalence of rheumatism." And: "Certain it is that we often see regiments exposed to damp, wet, cold, sudden and violent changes of temperature, and obliged to sleep on wet ground with but scant protection, and no cases of acute rheumatism" (Lehlbach, 1863). Nevertheless, rheumatic fever, if not as prominent among war diseases as we might expect, still causes no small proportion of medical casualties.

Campaign of Dettingen.—The earliest statistical information as to the incidence of acute rheumatism in a British and allied force in the field I owe to Sir John Pringle [1].

History repeats itself, and a British and allied force, the so-called "Pragmatic Army", leaving its winter quarters in Brussels in February 1743, marched into Germany, and was cantoned at Aachen and Julich, after experiencing its share of a widespread epidemic of influenza, and on May 17 encamped on the Maine in an open and healthful country. After three weeks of hot days and cold nights the "flying hospital" at Nied had 250 sick [1]. When the number had reached 220 the distempers had been classified and 51 were suffering from "rheumatic pains with more or less of fever". The Army numbered about 14,500 so the attack rate was about 3.5 per 1,000. Later in the summer the disease decreased, and became insignificant compared with dysentery and other intestinal diseases. On June 26 the Army, led by George II in person, won the battle of Dettingen.

Most of the cases were not of the very acute type, and it may be assumed that many myalgias were included, as has happened in more recent wars (*vide* Copeman *infra*).

Pringle clearly distinguishes between acute and more chronic rheumatism, points out the winter-early-spring maximum, and the importance of dry upland camping grounds. He considers most military sciaticas to be rheumatic, and found a "cold bath and riding" regime efficacious in the convalescence from some forms of chronic rheumatism.

It was in the Dettingen campaign that Pringle persuaded the Earl of Stair to propose to the French C. in C., the Duc de Noailles, that hospitals should not be fired upon. The Duke readily consented and ordered that his artillery should not fire on the village of Feckenheim, three miles from Hanau, in which the English field hospital was then lying with some 1,500 sick, mainly dysentery and typhus. This agreement was honoured by both sides throughout the rest of the campaign, thus anticipating the Red Cross movement (Henri Dunant, 1864) by a hundred and twenty-one years.

Pringle, who was also principal medical officer in the 1745 campaign ending in Culloden, came to London in 1748, was physician in ordinary to the Queen and F.R.C.P. in 1763. He was President of the Royal Society and an intimate friend of Captain Cook. His great work *Observations on the Diseases of the Army* (1752), with its modern appreciation of ventilation and space in hospitals and of hygiene generally, alone would secure him his celestial seat among the immortals of our illustrious profession, but his merits as a rheumatologist seem hardly to have been recognized.

I have found no military records of rheumatic fever in the Napoleonic wars. Even in the ill-fated *Walcheren* expedition of 1809, in which conditions might have been thought to favour a high incidence, and though 332 out of every 1,000 died of disease compared with 16 per 1,000 killed or died of wounds, I find no reference to rheumatic fever, so completely was it overshadowed by malaria and typhus fever. Things were very different as regards the ratio of disease and battle deaths one hundred and forty-two years later when our sons fought there once again.

Table I summarizes estimates from the various official histories of recent wars, estimates which are seldom strictly comparable. Those relating to the American Civil War of 1861-4 are especially misleading for, as the authors frankly point out, the contrast between the large incidence and the low death-rate, together with the low case-mortality, at a time when the latter in civil hospitals was about 3%, alike suggest that in this war the majority of cases assigned to acute rheumatism were in fact cases of fibrositis, myalgia or conditions other than acute rheumatism. Bearing in mind

TABLE I.—ACUTE RHEUMATISM IN MODERN CAMPAIGNS.

	Average annual incidence per 1,000 strength	Acute rh. admissions as a percentage of all non-battle admissions	Death-rate per 1,000 strength	Case-mortality %
Crimæa (British) 1854-6	24.5	3.2	1.16	4.7
American Civil 1861-4				
Union Army (Whites)	65.3*	4.7	0.20	0.44
Confederate	90*	3.6		4.0†
South African (British) 1899-1902	44	6.05	0.04	0.1
B.E.F. France 1915	35	3.9	0.03	0.1
Dardanelles (British) 1915	56	4.5	0.15	0.26
Italy 1918				
(British) Forward Area	0.27	0.07		
Troops in U.K. 1914-18	2.42	0.84		
British Army				
All areas 1917-19		0.32		
U.S. Army in U.S. and France 1917-19	2.14		0.01	0.18

* Much inflated with cases of muscular rheumatism, &c. [3b and c].

† Based on 1,984 cases in Richmond (Van.) (Chimborazo Hospital) [3a].

Copeman's ratio of 15% already referred to, it probably would be safe to divide the incidence of 65 per 1,000 by five or six.

The *Crimean campaign*, as everyone knows, was, in its first year, terribly mishandled. It began far too late in the autumn of 1854. There were great privations, severe exposure to frightful weather and much overcrowding. Great epidemics of cholera and typhus swept the armies, which, in the official medical history [2]—the first of its kind—so overshadow the canvas that one finds only two or three casual references to rheumatic fever in the "observations" and none in the texts of the regimental histories. It is only from the statistical returns that I have extracted the following facts. I was astounded to find that the case-mortality for the cases of chronic rheumatism, 6%, was higher than that for acute rheumatism, 4.3%. For the three months, December 1854, January and March 1855, the case-mortality of chronic rheumatism was nearly 19% compared with 12.2% for acute rheumatism and in one month, February 1855, the case-mortality ascribed to chronic rheumatism reached the astounding figure of 74.2%. I have, therefore, assumed in estimating the incidence, percentage of total admissions, death-rate and case-mortality, for *this war only*, that "chronic rheumatism" was here used to denote "subacute rheumatism" and have therefore included 1,135 cases (with 69 deaths) admitted for chronic rheumatism together with the 3,771 cases (with 163 deaths) admitted for acute rheumatism. Total admission for all diseases (excluding battle casualties) numbered 162,673. More than three-quarters of all the deaths occurred during the fearful weather of the three months of the "Crimean winter" of 1854-5 [2]. This followed close upon the great storm of November 14-15, in which eight ships bringing warm clothing, medical stores and food, sank and nearly all tents, hospital and other, and even huts were blown down. Both November and December were very wet and snow fell heavily. The case-mortality during these three months was 12.2%. From a sample of regimental returns (Table II) which I extracted, the

TABLE II.—CRIMEAN WAR: ACUTE RHEUMATISM IN THE BRITISH ARMY.

Two Years' Returns (from 11.6.1854) from a Large Sample of all Admissions to Hospital from 10 Cavalry Regiments, 3 Guard and 14 Line Infantry Battalions.

Arm	Total admissions for all diseases excluding battle wounds	Admissions for acute rheumatism	% of all medical admissions	Deaths	Case-mortality acute rheumatism
Cavalry	14,402	317	2.2	5	1.6
Guard	9,465	114	1.2	17	14.8
Line Infantry	32,359	567	1.75	30	5.3
Totals	56,226	998	1.77	52	5.2
Highest proportion					
1st Battn. 1st (Royal) Regiment	2,317	91	3.9	12	13.2
Highest case-mortality					
3 Gren. Guards	3,196	31	0.97	9	29.0

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diseases which included 1,076 cases of "rheumatism", 229 of myalgia and 18 of lumbago.

For 1916, 1917 and 1918 a sampling inquiry [6e] covered 18.5% of all admissions to hospital. Admissions for rheumatic fever formed 3.3% of the total admissions for all diseases and non-battle injuries. The rates for the same three years for troops in the United Kingdom were respectively 3.72, 2.24 and 1.46 per 1,000. The last is much the same as the estimated attack rate (1.53 per 1,000) for rheumatic fever in insured civilian males (16-24) in England and Wales in 1922 [8]. The 1917 incidence coincides with the American rate for troops.

American experience in the First Great War [5], April 1, 1917, to December 31, 1919.—There were 23,818 cases of rheumatic fever; the average annual admission rate was 2.2 for troops in the United States and France; the death-rate, 0.01 per 1,000, and the case fatality 0.18%.

During and immediately after the first Great War the military hospital admissions rate for acute rheumatism fell greatly and has since remained low, the Forces sharing with the civil community in the great and continuous reduction in the incidence and severity of rheumatic fever. The peacetime Army admission rate fell from 4.3 in 1913 to 1.7 in 1927; that of the Royal Navy from 7 per 1,000 to 1.7 for the same years. In 1927 the R.A.F. admission rate was 0.9. The American Army rate fell from 6.2 in 1913 to 1.1 in 1922.

The original *British Expeditionary Force* of 1939-40 which evacuated from Dunkirk had but little rheumatic fever. Copeman [7] records that during the first four months of this campaign admissions to base hospitals No. 2 and No. 3 for "rheumatic" conditions were about 15% of total admissions and 26% of all admissions in the medical division. But only 15% of these patients with "rheumatic conditions" (judging by the first 100 cases admitted to a special "rheumatism" ward) suffered either from acute or subacute rheumatic fever; the great majority—70%—suffered from fibrositis; 6% from rheumatoid arthritis and 9% from osteoarthritis (mostly traumatic in origin). Rheumatic fever therefore seems to have accounted for some 2.25% of total admissions to hospital.

Admission to E.M.S. hospitals from the Services.—Judging by the one-fifth samples taken by the E.M.S. Statistical Branch, Ministry of Pensions, Norcross, the numbers of patients from the Forces admitted to the E.M.S. hospitals [9] in this country with acute rheumatic fever in 1942 and 1943 show that the incidence was low, and that it was heavier in the first half-years than in the second half-years in each case, and that the proportion which rheumatic fever bears to the rheumatic group as a whole is not unlike that found in France by Copeman.

II. BARRACK OR TRAINING CENTRE EPIDEMICS OF ACUTE RHEUMATISM

Training centres often present the following features—a community of susceptible age rendered the more susceptible by sudden transference from home conditions to a strenuous regime, a rapid continuous influx of new entrants, sleeping quarters each containing many persons and overcrowded. At the appropriate season, the carrier rate of one particular (the "epidemic") strain of *Streptococcus pyogenes* rises, an epidemic of acute tonsillitis appears, and, a little later, cases of acute rheumatism, often in a ratio of about 1 to every 10 cases of acute tonsillitis [12]. Surgeon Commander C. A. Green [10] has reported one where the attack rate of rheumatic fever rose to 63 per 1,000. The recognition of this phenomenon is a matter of recent history, but if we look back some of the old records strongly suggest that it has often occurred before. Thus in 1859, when acute rheumatism admission rates in the Army were still high, that for depot battalions was 65.4 per 1,000, more than twice that for the Foot Guards, 31.7. It is recorded that "Many of the cases were the sequel of venereal disease" so the incidence shown is probably too high. The great differences in incidence [5] for white troops between the 32 training camps in the United States in 1917-19 suggest the probability of "barrack epidemics" in some of them. The average incidence for all these camps was 8.4 per 1,000, the highest 31.5 at Camp Cody, and the lowest 4.3 at Upton Camp. Table III shows some of the highest and the lowest but I have no information as to overcrowding or other features.

G. C. Ferguson (1943) describes a sudden increase in admissions to military hospitals in Canada for acute rheumatism in February, March, April and May 1942; 331 cases

Guards' case-mortality seems to have been ten times that of the cavalry who, not being in the trenches, were less exposed, and nearly three times that of those line battalions which are included in the sample. Perhaps the rigid discipline of the Guards kept the patients so long in the trenches after the onset of the disease that their recovery was prejudiced.

In this war the average annual incidence is more than usually misleading, calculated as it is on a strength of 98,000, for, at the beginning of the peak period, death, wounds and disease had reduced the effective strength to 24,000. In considering the high case-mortality, however, we must remember that in those days the average case-mortality in civil hospitals was reckoned as high as 3% (Loumis) [3c], and that in 1837 Macleod considered rheumatic fever "not only one of the most prevalent but one of the most fatal maladies incident to our precarious climate".

The fallacies of the *American Civil War* figures for the incidence of acute rheumatism have already been pointed out; and I regard the only figure worthy of credence to be the Confederate case-mortality which comes from a series of 1,984 cases "with known results" in the Chimborazo Hospital, Richmond, Virginia [3a]. The observations of the authors are, however, admirable and I have already quoted two extracts showing the unexpected rarity of the disease. A third acute observation is that: "Acute rheumatism shows in its monthly rates a greater prevalence in that period of the war during which new levies were sent to the field than later when the levies have become inured to the hardships of active service."

South African War 1899-1902.—In this campaign, characterized more by heavy marching on half rations than by severe battle casualties, the outstanding medical phenomena were the vast epidemics of typhoid and dysentery. But the admissions for rheumatic fever [6b] formed 6.05 of the total admissions for all diseases and non-battle injuries, and, during the whole war, amounted to 24,460, thus exceeding those for wounds, 21,292. The total killed and wounded was 27,273. The average annual admission rate was 44 per 1,000, the death-rate 0.04 per 1,000, and invalided 7.75 per 1,000. The case-mortality was 0.1%, half that of the American Civil War. If, however, the cases and deaths from *valvular disease* be included the case-mortality is 0.37%, which is doubtfully comparable with the American composite figure of 0.44 quoted above.

Why was there more rheumatism in the high and healthy climate of South Africa than in the mud of the trenches of 1915? One reason seems to have been that acute rheumatism had already begun to decline in incidence and severity. The heavy marching may have been an important factor in this war, and one often out-marched one's ox-drawn rations. Describing the march to Pretoria the author of the official military history [4] writes [The heavily laden infantry] "averaged nearly seventeen miles a day over apparently endless prairies in blazing sun and bitter cold, swept now by hot and choking dust storms, now by rushes of icy hail, fording rivers and floundering through sand, with scanty food and shelterless bivouacs, their toil had been almost unlightened by anything but hope. . . . On the vast levels there was nothing to be seen but their own long ranks, no sound to be heard but that of their own footsteps. Silence attended their marches, hunger, fatigue and discomfort their nightly sleeping places."

Great War 1914-19.—That rheumatic fever was less prevalent in France in 1915 with all its mud than in the magnificent climate of South Africa seems confirmed by the fact that after four years of trench warfare Colonel T. Hay [6a] wrote "acute rheumatic fever was not a common disease among soldiers in France, and it is improbable, therefore, that much valvular disease of the heart originated during war service". The vast majority of joint and limb pains in this war were due to trench fever and other non-rheumatic conditions.

It was not found practicable to deal with the medical casualties of the later years in the same detail as was done in 1915, and rheumatic fever is not included in the "principal recorded causes" of admission to hospital from the British Expeditionary Force in France for 1916 onwards.

In Italy [6d] the disease seems to have been very rare in British troops, 72 cases of rheumatic fever being admitted, thus making only 5.2% of the rheumatic group of

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Parrot [2] remarks that this ignorance of heart disease in antiquity may seem strange in view of the fact that other affections of less importance were thoroughly studied in ancient times, and suggests that the only explanation of this omission was that the heart was regarded as a sacred organ which it was wrong to touch and study. According to Moon [3] Aristotle, though he did not think the heart was exactly invulnerable, said that it was the only one of the viscera, and indeed of any part of the body, that was unable to tolerate any serious affection.

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TABLE III.—1917-1919 ACUTE RHEUMATISM (WHITES ONLY).

Variations in the Incidence in the 32 Training Camps of the U.S. Army. That these variations are not mainly climatic or geographic is suggested by comparison with the attack-rates in the States in which the Camps were respectively situated, but on other soldiers, who were not in the Training Camps.

Average attack-rate for enlisted men in U.S.: 8.12 per 1,000. Average attack-rate for whole U.S. Army and Europe: 6.43.				
Camp	Mean annual strength	Camp attack-rate per 1,000	State in which camp was situated	Attack-rate per 1,000 on non-camp soldiers in State
<i>High rates</i>				
Cody	22,636	31.5	New Mexico	8.50
Pike	40,869	19.4	Arkansas	8.82
Doniphan	26,747	18.4	Oklahoma	3.71
Funston	50,054	17.1	Kansas	29.40
Mean of all 32 camps.		8.4		
<i>Low rates</i>				
Lec	51,004	5.2	Virginia	4.22
Lewis	47,267	4.0	Washington	8.33
Upton	40,202	4.3	New York	6.9

Extracted from Vol. XV, Part 2, Med. Dep. U.S. Army in World War I.

were admitted in these four months, and 534 in the year ending July 31. This prevalence seems probably to have been due to something like "barrack epidemics", for 78% of the patients were between 18 and 25 years. The high carrier rate of *S. pyogenes* was shown by concurrent epidemics of scarlet fever and tonsillitis. The article demonstrates the military need (a need which has been particularly felt in the United States recently) to prevent such epidemics of acute rheumatism, for 50% of the patients were invalided out of the Service (including 35% with valvular disease and 7% with rheumatoid arthritis) while of the 50% who returned to duty, a further 20% were later invalided.

All statistics relating to acute rheumatism are difficult but to try to compare "invaliding" in the various wars leads only to a morass of differing phrases and differing meanings of the same phrase. It is clear, however, that the rates have greatly diminished in the last ninety years. I cannot hazard a guess for the Crimea. In the American Civil War the ratio was 25.1 per 1,000; in South Africa 7.75; in the first World War I estimate the figure at 8.2 per 1,000 but I do not think that this estimate relates so accurately to acute rheumatism as does the South African figure; it probably includes other forms than acute. It is yet too early for estimates for the Army in the present war. Surgeon Commander Green, however, tells me that in the one year 1944 in the Navy 0.26 per 1,000 were invalided for rheumatic fever with or without cardiac lesions, and an additional 0.08 invalided for allied cardiac conditions, making 0.36 per 1,000 (males) strength.

In the short time at my disposal I have tried to show that acute rheumatism, never acting a conspicuous part in military history, has always been an insidious foe especially to the recruit in training. Fortunately it appears an obsolescent disease in the Army as it is, as I have elsewhere shown [1], in civil life. This cheering impression of a rapid decline should stimulate our efforts finally to extinguish this Moloch of young life and health.

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INTRODUCTION

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Therapeutic and prophylactic action of the heart.—Not only have numerous popular remedies been used in the treatment of various forms of cardiac disease, but in many instances the heart itself in man and animals as well as heart-shaped inanimate objects have been credited with prophylactic and curative properties, of which the following are examples:

Dingwall [10] relates the case of "a man in Kenlochewe, who was told by a wise woman that his cattle suffering from pestilence would only be cured if he got the heart of a man who did not know his parents, dipped it in a bucket of water and sprinkled the cattle with the water. A pedlar came his way shortly afterwards. He murdered him, got his heart, and cured his cattle, but the disease was transferred to his family, and their descendants, with this taint of madness, were to be recognized less than a hundred years ago".

According to Democritus quoted by Pliny [11a] the chameleon's heart attached to the body with black wool of the first shearing is a good preservative against attacks of quartan fever. Democritus [11b] also states that a quartan fever is effectually cured by attaching a crocodile's heart to the body with the wool of a black sheep without a speck of any other colour, due care being taken that the sheep was the first lamb weaned by the dam.

Another cardiac remedy for fever, mentioned by Pliny [11c], is to swallow the heart of a sea-diver removed from the bird without the aid of iron, it being first dried and then bruised and taken in warm water. The heart of a swallow with honey is also recommended, as well as a viper's heart removed from the reptile while still alive [11c].

Seligmann [12] relates that in Ancient Egypt one form of protection against the Evil Eye consisted of a drop of water and the urine of an ape combined with the heart of a jackal, a stalk of grass and the nose of a pig.

It is noteworthy in this connexion that in Roman Catholic countries, and especially Portugal, amulets in the form of a heart are extensively used as a prophylactic agent against the Evil Eye [13].

According to *Arcana Fairfaxiana Manuscripta* [14], of which the subtitle is "A manu-

script volume of Apothecaries' Lore and Housewifery" nearly three centuries old, used and partly written by the Fairfax Family, a cure for the falling sickness (epilepsy) is as follows: "Take the harte of a toade and drie it and beate it to powder; then drinke with what drinke you will."

According to Pliny [11d] "some say that the heart of the lark should be attached to the patient's thigh for the cure of colic and according to others the heart should be swallowed fresh, quite warm in fact. There is a family of consular dignity, known as the Asprenates, two brothers, members of which were cured of colic, the one by eating a lark and wearing its heart in a golden bracelet, and the other by performing a sacrifice".

As regards the prophylactic action of the heart Pliny [11e] quotes the statement that persons who carry the heart of a vulture about them will be safe not only from serpents but from wild beasts as well as robbers and will have nothing to fear from the wrath of kings.

Besides its therapeutic action, there are several other results of the administration of the heart, as is shown by the following examples among the "prodigious lies" of the magicians mentioned by Pliny [11f]: "They pretend that the heart of a horned owl applied to the left breast of a woman while asleep will make her disclose all her secret thoughts."

In this group may be placed those recorded by Bonnerjea [15]: (1) In East Prussia there is a belief that if the heart of an unborn child is carried on the person it is sure to bring about complete success in the thieving profession. (2) The Jews of Minsk believe that if a person eats the heart of a bear he will become a tyrant.

Speaking of the mole, Pliny [11g] remarks that of all animals it is the mole that the magicians admire most. There is no animal in the entrails of which they put such implicit faith. "So much so, indeed, that if a person swallows the heart of a mole fresh from the body and still palpitating, he will receive the gift of divination, they assure us, and a foreknowledge of further events."

In George Wales' *Book of Cures* quoted by Mrs. Gutch [16] we read "if any one swallow the heart of a swallow, or a weasel, or a mole while it is still warm with natural heat, it shall help him for remembering, understanding and foretelling".

Pliny [11h] quotes Democritus to the effect that "if a tongue is extracted from a live frog, with no other part of the body adherent to it, and is then applied—the frog being first replaced in the water—to a woman while asleep, just at the spot where the heart is felt to palpitate, she will be sure to give a truthful answer to any question which may be put to her".

FOLK-LORE SUPERSTITIONS CONNECTED WITH THE HEART

According to Pliny [11k] "it is asserted that the heart cannot be burnt in those persons who die of the cardiac disease and that the same is said of those who die by poison". In support of this view Pliny quotes the case of Vitellius who accused Piso of poisoning Germanicus, and in support of this accusation declared that the heart of Germanicus could not be burnt. On the other hand the peculiar nature of the disease from which Germanicus suffered was alleged in Piso's defence.

Although Pliny's work contains more folk-lore than any of his contemporaries, Moulé [17] suggests that his lack of confidence in many of the remedies he mentions is shown by the frequency with which he uses the words "ut aiunt", "ut tradunt", "dicitur" and "dicuntur" in the description of various remedies.

Another popular belief mentioned by Pliny [11m], for which there does not appear to be any foundation, is that animals with a hard and rigid heart are looked upon as stupid and lumpish, while those in whom it is small are courageous and those with a very large heart are timid.

Casting of the heart.—In Orkney and Shetland according to Black [18] and Gregor [19] the inhabitants firmly believe that if any person is emaciated by sickness or other accidental causes the heart is worn away. The method of determining this is known as *Casting of the Heart* and carried out by melting a piece of lead and throwing it into cold water. According to the shape it takes, so they form their judgment. If it takes the shape of a heart, the person is not altogether gone and will recover.

The heart and insanity.—In Highland therapy as Mrs. Moodie [20] has shown, there was a belief that insanity was caused by a person's heart getting displaced, owing to a sudden shock. It was imagined that a similar sudden shock would replace it in its former position, and that thus the natural balance would be restored. Consequently a sudden shock was one of the old specifics for insanity.

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Section of Proctology

President—ERIC A. CROOK, M.Ch.

[November 14, 1945]

Non-specific Intestinal Granuloma

PRESIDENT'S ADDRESS

By ERIC A. CROOK, M.Ch.

For many years it has been recognized that certain tumour-like formations occur in both large and small intestines which do not conform to any known specific pathology. This group of lesions, showing massive new formations of tissue, was originally put in a separate category from neoplastic conditions and contained in its number lesions which have subsequently, in their turn, been split off from the main mass on the discovery of their specific pathology. A group of undetermined pathology still exists, possibly not all similar in aetiology, for which the term "non-specific intestinal granuloma" appears the best to adopt, as the more generally accepted term "infective granuloma" implies an infective nature of which we have at present no proof.

Before the year 1907 there are occasional references in the literature to tumour formations in the bowel that did not present the features of new growth, but it was in this year that Lord Moynihan described the condition giving details of six cases in a paper entitled "The Mimicry of Malignant Disease of the Large Intestine". Two of these cases involved the rectum, with thickened walls, causing stenosis and ulceration of the mucosa. Two involved the sigmoid colon with tumour formation and "false diverticula". Two affected the transverse colon, forming a hard smooth tumour mass which disappeared after a short-circuiting operation.

In 1909 Braun gave a report on these non-malignant tumours, and in the same year le Dentu described similar cases under the heading of "False Cancers and Inflammatory Tumours of the Abdomen". He subdivided these into groups: (i) interstitial colitis, circumscribed in character and associated with hypertrophy, resulting in a certain amount of stenosis; (ii) simple pericolicitis with adhesions; (iii) diffuse pericolicitis with the formation of an elongated mass; (iv) exuberant pericolicitis, in which form the intestines and extra-peritoneal connective tissue and glands are all matted together.

Isolated cases of tumour formation associated with diverticula of bowel were recorded at this time, and the condition of diverticulitis came to be recognized, with its established pathology, thus detaching itself from the main group of non-specific granulomata. The earliest comprehensive account of diverticulitis is given by Maxwell Telling in 1916,

Displacement of heart and sudden death.—Another effect of cardiac displacement also supposed to occur in the Highlands, according to Rorie [7b], was sudden death, especially in pregnancy or severe scalding in a child. In the case of the mother sudden death was attributed to "the bairn pittin' up its hand and grippin' its mother's heart".

In the mining folk of Fife, according to Rorie [7c], hiccough is supposed to be caused by "a nerve in the heart" and at every hiccough "a drop of blude leaves the heart".

According to Elworthy [21] the County Museum at Taunton contains several hearts studded with pins, said to be those of pigs and found long ago in old houses. Besides being protective the hearts were supposed to possess evil properties and to have a malignant effect on the person in whose house they were found. It was believed that the hated person's heart would suffer from the pricking inflicted upon the pig's heart and that as the latter dried up so would the heart and life of the victim against whom the act was directed.

In his *Vulgar Errors* (IV, 4) Sir Thomas Browne shows that there is no anatomical foundation for the belief that there is a small vein, nerve or artery running from the left finger to the heart. Reference may be made here to the celebrated "Voltaire's Nerve" which is an imaginary nerve running from the brain to the organs of generation via the eyes, lips and heart. As I have suggested elsewhere [22] this conception was not a mere *jeu d'esprit* in view of the fact that the role of the nerves in the economy was still in the realm of nebulous hypotheses in Voltaire's day, and it was not until the time of Charles Bell in 1811 and Magendie in 1812 that the functions of the nerves were well understood.

Eating the heart.—MacCulloch [23] remarks that as the heart is regarded as the seat of life, soul, wisdom and similar virtues, savages devour the hearts of their enemies so that these qualities may pass into them. This practice is sometimes combined with the eating of other parts of the body, especially the liver, which was credited with similar qualities. Some animals, particularly the lion, bear, wolf and certain birds such as hawks or crows, are also treated in the same way for the purpose of transmitting strength, courage, cunning, wisdom, &c.

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re of these fistulæ. He gave no explanation of the ætiology of the process, which did fall into any of the recognized granulomatous or accepted inflammatory groups. No circle bacilli were found, and the Wassermann reaction was negative. There were no significant agglutination titres against the various strains of dysentery organisms, and its intradermal test was negative. The disease ran a relatively benign course, and the sufferers who survived operation were restored to good health. He based observations on a study of 14 cases. In his description of the tissue changes, describes the mucosa as presenting a cobblestone appearance, replacing the normal intestinal folds. A series of small linear ulcerations is found in a groove on the mesenteric side of the bowel, which may be remnants of the original ulcerative lesions that led to the bullous change in the mucosa, or possibly mechanical erosions due to the formation of a *Darmstrasse* produced by shortening of the fibrotic mesentery. The mucosa and, to a less extent, the muscular layers of the bowel are the seat of marked inflammatory hyperplastic and exudative changes and the wall of the bowel becomes enormously thickened, and presents the appearance of a hosepipe at operation. In later stages the exudative reaction is replaced by a fibrostenotic process, the mucosa appears opaque with occasional islands of polypoid overgrowth. The serous coat loses its gloss and may have tubercle-like structures on its surface. The mesentery is greatly thickened and fibrotic, and the glands are enlarged. There is a tendency to slow perforation with resulting adhesions and fistulæ, especially to the sigmoid and ascending colon. Walled-off abscesses form which are often thought to be appendicular in origin, and if they are opened they lead to fecal fistulæ. Microscopically, there are no specific features but varying degree of acute, subacute and chronic inflammation, in which giant cells of the foreign-body type may be seen.

Borke and Lee put forward the view that the tissue changes were produced by a secondary involvement of the blood supply, due to lymphangitis, which lead to a slow vitalization of the bowel wall, and recently Reichert and Mathes (1936), struck by a marked œdema and fibrosis of the intestinal wall and lymphatic engorgement present in resected specimens, attempted to reproduce the disease experimentally. They blocked the mesenteric and subserous lymphatics of dogs by injection and gave intravenous injections of *B. coli*. In this way they produced a chronic lymphœdema of the ileum and appearances somewhat resembling Crohn's disease.

Following Crohn's original article, a large number of cases conforming to his description are published in the journals. A case described by Colp (1934) is of interest. The patient, a medical student, was operated on for appendicular colic, and at the time of the operation, appearances of Crohn's disease were noted involving the terminal ileum and cæcum. The appendix and glands were removed and reported by the pathologist to be normal. He derived no benefit from the operation, and returned to hospital in eight weeks when a mass could be felt in the right iliac fossa. This case supports the view that the disease does not only elect and affect the ileum, but may attack the cæcum and other areas of the colon. The ileocæcal valve does not arbitrarily limit the downward progress of the disease affecting the ileum, any more than it limits the upward progress of ulcerative colitis. In the many cases recorded there is great variation in the condition present.

A case of massive intestinal hæmorrhage in Crohn's disease is recorded by Fallis (1941).

In 1939 Crohn accepted the possibility of the condition involving the cæcum as well as the terminal ileum, and of occurring in isolated segments of the colon. He did not consider trauma played a part, and did not incriminate the appendix. He referred to the association of perianal and rectal fistulæ, which he considers occur as a result of infection in the rectal crypts of Morgagni by contaminated fecal material. He mentioned fistula-in-ano as occasionally being the presenting symptom in regional ileitis, before the abdominal lesions could be detected, and he quotes the instance of a house surgeon examining a patient admitted to hospital for operation on fistula-in-ano, and finding a mass which suggested and subsequently proved to be Crohn's disease, previously unsuspected. In the treatment he found that a simple short-circuit operation gave a 50% recovery, so he favoured resection of the affected tissue, carrying this out in one stage, if possible. Resection, however, was sometimes followed by recurrence.

Hadfield (1939) gave an account of the histology of Crohn's disease, considering it to be a lymphadenoid hyperplasia with the formation of non-caseating giant-cell systems in the submucosa. He finds the lesion also present in the lymph glands. Ulceration and fistulæ he considers to be secondary to the lesion in the submucosa, and the obstructive lymphœdema which it produces. Ulceration often obscures and sometimes obliterates the primary lesion in the submucosa, and when this happens he finds that the lesion is not uncommonly present in some or all of the regional lymphatic glands.

and even at this time he comments on the fact that the condition had not yet reached the ordinary students' textbooks of Surgery.

After this, little reference to "granuloma" is found in the literature till 1923, when Moschowitz and Wilensky published an article, "Non-specific Granulomata of the Intestine", describing four cases, three of these in the cæcum and ascending colon, and one at the splenic flexure. In two cases the appendix had been removed previously in a state of acute inflammation, and in the third the appendix showing signs of chronic inflammation was found in the mass. In all three specimens there was a firm tense uncircumscribed tumour, involving all the coats of the intestine, and causing constriction of the lumen. In three cases there were superficial ulcerations of the mucosa. In one specimen the main bulk of the tumour projected into the mesentery. In another specimen a granuloma of the small intestine had developed a year later, after resection of the ascending colon.

Microscopically these cases gave almost identical findings, viz. interstitial infiltration of all the coats of the intestine, with round cells and plasma cells, and there was wide variation of a fibroblastic formation from a comparatively richly cellular tissue to a firm tense fibrous scar. There was new blood-vessel formation. Giant cells were present, especially in the specimen from the small intestine. No tubercle bacilli were found and no caseation. Wassermann reaction was negative.

In 1925 Frei proved the specific infective nature of certain granulomata in the rectum by his intradermal test. His antigen consisted of the filtrable virus obtained from a bubo in a known case of lymphogranuloma inguinale. Another granuloma of specific pathology was thus established, and became detached from the main non-specific group.

In 1931 Mock gave a full description of this condition, which he calls "Infective Granuloma". He considered these tumour-like masses to be influenced to a certain extent by a low-grade non-specific infection, and characterized by a piling up of granulation tissue showing varying stages of necrosis, fibroblastic changes and the true scar tissue, or reparative tissue growth. These masses, usually not well circumscribed, often reach the size of an orange, a grape-fruit, or occasionally a child's head. They are not specific granulomata. He considered the underlying cause to be some local interference with the blood supply, followed by a small area of necrosis, followed in its turn by a reparative tissue reaction. Low-grade organisms may be present at the start causing this interference with the blood supply and resulting tissue changes, or the inflammatory mass may arise first and be attacked subsequently by pyogenic organisms. He grouped the causes under three headings: (1) Conditions existing within the gastro-intestinal tract itself, or its mesentery, considering the hypertrophic mass that may develop at the site of a gastric ulcer as comparable; (2) extraperitoneal infections which gradually spread to and involve the gastro-intestinal tract, such as retroperitoneal adenitis, causing a necrotic mass; and (3) trauma, which may be produced by external injury, affecting the mesentery or intestine; partial volvulus or constriction in a hernial sac, foreign bodies or ligatures that cause interference with blood supply. The symptoms he grouped in three headings: (1) Those attributable to the inflammatory process; (2) those due to obstruction, and (3) those that are constitutional. In the treatment he advocated excision of the affected tissues, but he recognized the fact that in many cases the mass disappears after a short-circuiting operation. He stresses the importance of taking a portion of tissue for microscopic section, if the whole lesion is not to be excised.

In the following year, 1932, Crohn published his description of regional ileitis, which he considered a clinical and pathological entity that could be split off from the general mass of non-specific granulomata. He describes a disease of the terminal ileum affecting mainly young adults, characterized by a subacute or chronic necrotizing and cicatrizing inflammation. The ulceration of the mucosa is accompanied by a disproportionate connective tissue reaction of the remaining walls of the intestine, a process which frequently leads to stenosis of the lumen of the intestine, associated with the formation of multiple fistulae. The clinical features of the disease he considered to resemble most closely those of ulcerative colitis, fever, diarrhoea and emaciation, leading eventually to an obstruction of the intestine, the constant presence of a mass in the right iliac fossa usually requiring surgical intervention.

In this original description he stated the condition was limited to the terminal ileum, the process beginning at, and involving in its maximal intensity, the ileocaecal valve, tapering off gradually as it ascends the ileum for 8 to 10 in. The familiar fistulae lead usually to segments of the colon forming small tracks, communicating with the lumen of the large intestine. Occasionally the abdominal wall anteriorly is the site of one or

C. F., woman aged 23. Her symptoms were pain in the right side and diarrhoea, and a tumour in the right iliac fossa was found on examination. At operation the terminal ileum and its mesentery were found to be thickened. Resection was carried out, and the tissue showed naked-eye and microscopic appearances of Crohn's disease.

The interest in this case lies in pain and diarrhoea being the initial symptoms and a tumour being present.

F. D., woman aged 44. She stated she had been admitted to hospital in 1927, with pain in the right side of the abdomen and vomiting. The diagnosis of appendix abscess was made and the late Mr. Russell Howard operated and according to reports found a matted mass in the right iliac fossa consisting of oedematous caecum and ileum. The appendix was not seen. The wound healed by first intention. She was admitted to hospital five months later and an abdominal abscess was drained. Two years later, 1929, cholecystectomy was performed for gall-stones, and the appendix was removed. Following this operation the patient says she kept fairly well, except for occasional pains in the stomach, until 1936, when she noticed a gradually increasing frequency of micturition and attacks of diarrhoea. After eating tomatoes she noticed the soft pips in her urine. She was admitted to a nursing home and a tender hard mass was felt in the right iliac fossa. A catheter specimen of urine contained intestinal material and a barium meal showed ileocolic and ileo-vesical fistulae. At the operation a large thickened loop of ileum was found lying on the bladder, with a communication between the ileum and the bladder, in an area acutely inflamed. The ileum terminated in a mass of adherent tissues containing caecum and ileum in the right iliac fossa. The appearances were those of the then recognized Crohn's disease. The ileum was detached from the bladder, openings in ileum and bladder were closed, and omentum was sutured between the two viscera. The patient made a good recovery, got strong again and felt well after this operation, for a year. Periods of ill-health then returned with abdominal pain and frequency of micturition, with fibres in the urine.

I saw her first in February 1944, when she complained of increased frequency of micturition, and colicky abdominal pains. She was a thin, pale woman, the abdomen was distended and peristaltic waves were clearly visible. There was tenderness in the right iliac fossa but no mass could be felt. The urine contained pus cells, meat fibres and vegetable cells. It was clear that a communication existed between the ileum and the bladder, and that partial obstruction of the intestine was taking place. At the operation, I found a scarred mass in the right side of the pelvis binding down lower ileum to bladder. The ileum was dilated and numerous inflammatory patches were present in its wall. I joined ileum to ascending colon and did not disturb the mass. She made a satisfactory recovery. The urine cleared up before she left the nursing home, and there was no further abdominal discomfort. She has subsequently steadily gained weight and had no recurrence of symptoms.

The interest in this case lies in the recurrence of the ileo-vesical fistula after the careful and thorough closure, which suggests that the pathological process at work in Crohn's disease is an infective one.

Comment.—If any inference can be drawn from such a short series of personal cases it is perhaps the very varied clinical picture that these intestinal granulomata do present. In two of my cases severe haemorrhage was the chief symptom. In two of them fistula, and in one abdominal pain, and the presence of a tumour.

There is no clear pointer to the aetiology but an infective origin is suggested by the fact that the active pathological process continued after operative treatment, which probably did not completely remove the lesion.

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Sir Philip Manson-Bahr: *Crohn's disease: Chronic cicatrizing enteritis: Regional ileitis.*—It is necessary to study the characteristics and implications of this disease of the small intestine, for there are reasons to believe that it may on occasions extend to the colon as well.

The credit for the first description of regional ileitis is usually accorded to Crohn. Ginzburg and Oppenheimer in 1932, though it is now pointed out that an accurate

SUMMARY

It is clear to us now that non-specific intestinal granuloma, when first recognized, constituted a mass of conditions of undetermined pathology. In the course of time lesions of determined pathology were split off the mass, such as diverticulitis and lympho-granuloma. We are left with a condition affecting mainly the ileum, and less frequently the colon, and the problem of its aetiology has not yet been completely solved.

The histological appearances and the liability to recur after operation appear to point to an infection, the true nature of which is at present unknown. In two of the cases in this short series that I am about to describe, this view appears to be supported.

CASES

This short series of cases that I have had—5 only in the past five years—are of interest in showing the different clinical pictures that the condition may present.

D. T. D., aged 49. I was first called to see him in November 1937 for a sudden severe rectal hæmorrhage, so severe as to endanger life. He subsequently regained his normal health, but some months later, another, but small hæmorrhage, took place. Sigmoidoscopy showed darkish blood coming from above the reach of the instrument. Barium enema X-ray was interpreted as showing colitis and an ulcer in the iliac colon. Laparotomy was advised, but after a further opinion, medical treatment was adopted—a period of rest in bed and a non-roughage diet. His general health was fairly good till 1940, when he had an attack of acute pain in the left iliac fossa. Examination revealed a tender mass that was thought to be a diverticulitis, or possibly colon carcinoma with peritoneal involvement. At operation in June 1940, the mass was found to be thickened descending colon. It was resected and an end-to-end anastomosis carried out, and a safety valve cæcostomy established. The pathologist's report on the tissue was Crohn's disease. The wound did not heal by first intention, and a purulent discharge persisted.

In 1942 a transverse colostomy was established, and the original wound then healed. The interest in this case was the hæmorrhage as the initial symptom. Pain and tumour were later manifestations. The persistent suppuration after the resection seems to suggest that the condition was infective and was not completely removed at operation.

S. D., man aged 49. He was admitted to hospital in March 1940 with symptoms suggesting a grumbling appendix, that had become more acute recently. There was a tender swelling in the right iliac fossa. At operation an abscess was found and an inflammatory mass involving the appendix. The appendix was removed, and the wound drained. The pathologist reported that he found no abnormality in the section of the appendix. The pus showed no tubercle bacilli and the culture yielded growth of micrococci only. The wound healed slowly but soundly. Thirteen months later he was readmitted to hospital, with pain in the right iliac fossa and a tumour, the size of an orange. An abscess was found and drained. The wound was slow in healing. Three months later the wound broke down, and a sinus formed. No specific organisms were found in the discharge. A laparotomy was performed and thickening of the terminal ileum found. Resection of the terminal ileum, cæcum and ascending colon was carried out. The wound healed well. Examination of the portion of terminal ileum removed showed the typical appearances of Crohn's disease, and this was confirmed by microscopic section.

The interest in this case lies in the mistake in the diagnosis in the first place, the recurrence of the suppuration suggesting that the early symptoms were wrongly attributed to the appendix. The initial symptoms were pain in the right side and the presence of a tumour.

M. L. M., woman aged 25. Her appendix had been removed some years previously. One year before admission she had passed a considerable amount of dark blood from the bowel on one occasion. On admission to hospital, an ill-defined mass was felt in the right iliac fossa. At operation an abscess was found beneath the abdominal wall, and in the centre of it was a piece of silkworm-gut. Some thickening of the ileum was noted, and a small portion taken for microscopic section. Cultures of the pus gave *B. coli* and no tubercle bacilli or streptococci or *Streptothrix actinomycetes*. The microscopic appearances of the tissue were suggestive of Crohn's disease. The wound healed and the patient made a good recovery. She went home and kept well for six months when a severe rectal hæmorrhage occurred and she was readmitted to hospital. Her hæmoglobin had dropped to 22%. This was restored to normal limits by giving her blood, but another hæmorrhage took place during her recovery.

A diagnosis of regional ileitis was made and a laparotomy performed. The terminal ileum was found to be thickened and a resection was carried out. The appearances of the tissue and the microscopic section confirmed the diagnosis of Crohn's disease. The foreign body, the portion of silkworm-gut, had apparently been in the tissues since the previous operation five years before and, though probably responsible for the abscess that surrounded it, could not be considered the cause of the granulomatous condition of the bowel, in the light of the histological findings.

The interest in this case lies in there having been a previous appendicectomy, in the discovery of a foreign body in the abscess, and the bleeding being the initial symptom.

Blackburn *et al.* (1939) thought that the giant cell systems were indistinguishable from those of tuberculosis. Cutler (1939, *N.Y. St. J. Med.*, 39 (i), 328) tested out his cases with Johnin, a by-product of the growth of the pseudo-tubercle bacillus of cicatrizing enteritis of cattle, but his results were negative.

(2) *Lymphogranuloma inguinale*.—The general form of the lesions in the large bowel, when these are encountered, bears a resemblance to the intestinal phenomena of lymphogranuloma as noted by Stafford (1938, *Johns Hopk. Hosp. Bull.*, 62, 399) and by James (1938, *Brit. J. Surg.*, 25, 511) who recorded a case in which the colon alone was involved. Likely and Lisa (1939, *Amer. J. Digest. Dis.*, 6, 113) found at autopsy multiple granulomata of the ileum and colon together with the genito-ano-rectal syndrome in a negress. The resemblance in this case extended to the histological appearances which in lymphogranuloma inguinale also consist of a lymphatic hyperplasia. However, Stafford (1938) tested out three of his regional ileitis cases with Frei antigen with negative results. My aim here is to point out that that form of non-specific granuloma of the colon which is treated at some length in American literature is probably identical with Crohn's disease. The term "granuloma" is applied to tumour-like inflammations of the colon not due to any demonstrable organism. There is described pericolic inflammation of low-grade type, which, whilst not causing any marked reaction in the intestine itself, yet brings about a hyperplastic reaction in the adjacent omentum until the thickening involves the wall in a tumour-like formation. The adjacent lymphatic glands become implicated. There may be, as in the ileum, mucosal ulcers.

Many of these granulomatous tumours occur in the region of the cæcum and may closely mimic a malignant tumour. Microscopically this granuloma resembles a mass of granulomatous tissue and consists of the same cellular elements, including Langhans' giant cells containing crystalline bodies (Rankin, F. W., Bergen, J. A., and Buie, L. A., 1935, "The Colon, Rectum and Anus", p. 207, Philadelphia and London).

(3) *Phlegmonous enteritis*, originally described by Rokitsansky (1842), has the same pathology as that of Crohn's disease as pointed out by Clark and Wright (1937). Its resemblance to phlegmonous gastritis has already been commented upon.

(4) *Dysentery*.—Felsen (1936) claimed from a correlated study of 553 cases that both acute and chronic ileitis might result and that this pointed to a common ætiology. He claimed to have obtained positive cultures of *B. dysenteriae*, Flexner and Sonne, during the acute stages and positive agglutination tests in the chronic. There has been no confirmation from other sources.

(5) *Sarcoidosis of Boeck*.—Williams and Nickerson first suggested that chronic ileitis might be related to sarcoidosis. With this object in view they emulsified a skin lesion from a proven case of sarcoidosis which gave positive intradermal reactions in two other cases of sarcoidosis and also in two of regional ileitis.

Sarcoidosis is identical with benign lymphogranulomatosis first described by Schaumann in 1914 (Hadfield, C., and Garrod, L. P., 1942, "Recent Advances in Pathology", p. 46, London). The histological picture (as in Crohn's disease) consists of large pale-staining cells of the endothelial type arranged in follicles resembling miliary tubercles as in some of them there is a centrally or laterally placed giant cell of the Langhans' type. I would like to suggest for future investigation that the virus which produces these lesions might be related to that of lymphogranuloma inguinale (which also gives rise to a similar cell picture). The difficulty surely consists in isolating this virus from intestinal and contaminated lesions. Ravant, Levaditi, Lambling, and Cachera (1932, *Bull. Acad. Méd., Paris*, 107, 3, 97) overcame this successfully in the case of lymphogranuloma inguinale by inserting a portion of the rectal stricture under the skin of guinea-pigs, subsequently dissecting out the enlarged lymphatic glands which contained the virus in a pure state, making an emulsion of them, and injecting this intracerebrally into white mice and monkeys, thus producing the typical encephalitis. In this manner the virus was isolated and transmitted in a pure state.

(6) *Lymphatic obstruction*.—Reichert and Mathes (1936), by injecting various sclerosing agents into the mesenteries and subserosal lymphatic channels and at the same time introducing bacteria intravenously, were able to produce œdema and extensive infiltration of the bowel wall. They concluded that regional ileitis was none other than a low-grade lymphatic infection, but Barrington-Ward and Norrish (1938, *Brit. J. Surg.*, 25, 530) suggested that disease of the mesenteric glands might be primary and that the ileitis might be due to the lymphatic block.

(7) *Infection through the mucosa*.—Although attempts have been made to identify organisms by aerobic and anaerobic cultures there are few reports of successful results,

account was given at the beginning of the last century by Combe and Saunders before the Royal College of Physicians, London, under the title of: "A singular case of stricture and thickening of the ileum."

Since 1932 a great literature has been built up around this disease. Approximately 160 papers dealing with this condition are listed in the *Cumulative Index* during the years 1939-1943. Shapiro, reviewing the literature in August 1939, tabulated 519 cases of regional ileitis in whom operative measures had been carried out (*Amer. J. med. Sci.*, 1938, 269).

Regional ileitis usually and mainly affects the terminal portions of the ileum; it sometimes also extends to the jejunum and ileocecal region. There is some evidence that circumscribed granulomata (so far known as non-specific granuloma) in the colon are of the same nature, as will be detailed later.

The regional lymphatic glands are enlarged and there is also thickening of the mesentery. Up to 1934 almost all recorded cases were to be found in the American literature, but since then there have been numerous references in English medical journals. The disease is more common in males and in Crohn's original series there were more than twice as many males as females. Originally described as affecting chiefly young adolescents, cases have been reported involving all ages.

The best and most recent account of the pathology is by A. Lyall (1945, *Glasgow med. J.*, 25, 1).

Pathology.—Two or more areas of the bowel may be rarely involved. The lengths of uninvolved bowel separating these areas are often called "skip areas". Blackburn and his co-workers (1939, *Bart's Hosp. Rep.*, 72, 181) speak of a "specific response" which they observed in 13 out of 20 cases. They noted marked hyperplasia of the lymphadenoid tissue in the submucosa producing cellular masses measuring 3 mm. in diameter; in some of these follicles the so-called "specific response" was seen and the germinal centres were replaced by proliferating endothelial cells. A basic problem which arises in the study of the pathology is whether this condition is chronic like tuberculosis or whether the early stages correspond to those of phlegmonous gastritis to which it bears some resemblance. As will be readily realized emphasis is laid on the histology as suggesting the identity of these various lesions.

The pathology can be divided into various stages:

(a) *Stage of acute suppuration.*—The affected length of the bowel is dark red in colour, greatly thickened and there are usually yellow shreds of fibrin adherent to the inner mucosa. The near-by glands are enlarged and red in colour. There is free, sometimes turbid, fluid in the peritoneal cavity. Miliary abscesses sometimes found in the submucosa resemble those seen in full-blown phlegmonous gastritis.

(b) *Chronic stage.*—Descriptions of this stage are commonly found in the literature. The naked-eye appearance of the affected bowel is typical and corresponds to Dalziel's simile of "an eel in a state of rigor mortis" or more commonly referred to as the "hose-pipe appearance". The serous surface of the bowel has a greyish-pink colour with white thickened patches representing organized fibrin. The terminal portions of the affected loop are often affixed to the pelvic brim by recent adhesions.

(c) *The fibro-stenotic stage.*—In this the cellular structure has been largely replaced by fibroblasts which have laid down collagen fibres and these have produced marked narrowing of the area. It is this stenosis which gives rise to the radiographic "string sign of Kantor". As this constriction advances the blood and lymphatic supplies of the bowel become interfered with and widespread ulceration of the mucosa takes place.

(d) *Fistula formation.*—As originally pointed out by Crohn there is a marked tendency to the formation of fistula and this may precede even the initial symptoms. These fistulae sometimes travel a long distance before reaching the surface. It has been suggested that they may be of chemical origin due to the action of the intestinal juices or possibly to the virus of lymphogranuloma inguinale.

Ætiology.—(1) *Tuberculosis.*—The chronic stages of Crohn's disease have certain resemblances to tuberculosis of the hyperplastic type, but no subserous tubercles have ever been demonstrated. That the disease is progressive like that of tuberculosis is seen by the fact that in some cases in which resection of the ileocecal portion has been performed the disease has subsequently reappeared in the ileum. Every effort made by different investigators to demonstrate tubercle bacilli, mainly by injection of material into guinea-pigs, has signally failed.

Blackburn *et al.* (1939) thought that the giant cell systems were indistinguishable from those of tuberculosis. Cutler (1939, *N.Y. St. J. Med.*, 39 (i), 328) tested out his cases with Johnin, a by-product of the growth of the pseudo-tubercle bacillus of cicatrizing enteritis of cattle, but his results were negative.

(2) *Lymphogranuloma inguinale*.—The general form of the lesions in the large bowel, when these are encountered, bears a resemblance to the intestinal phenomena of lymphogranuloma as noted by Stafford (1938, *Johns Hopk. Hosp. Bull.*, 62, 399) and by James (1938, *Brit. J. Surg.* 25, 511) who recorded a case in which the colon alone was involved. Likely and Lisa (1939, *Amer. J. Digest. Dis.*, 6, 113) found at autopsy multiple granulomata of the ileum and colon together with the genito-ano-rectal syndrome in a negress. The resemblance in this case extended to the histological appearances which in lymphogranuloma inguinale also consist of a lymphatic hyperplasia. However, Stafford (1938) tested out three of his regional ileitis cases with Frei antigen with negative results. My aim here is to point out that that form of non-specific granuloma of the colon which is treated at some length in American literature is probably identical with Crohn's disease. The term "granuloma" is applied to tumour-like inflammations of the colon not due to any demonstrable organism. There is described pericolic inflammation of low-grade type, which, whilst not causing any marked reaction in the intestine itself, yet brings about a hyperplastic reaction in the adjacent omentum until the thickening involves the wall in a tumour-like formation. The adjacent lymphatic glands become implicated. There may be, as in the ileum, mucosal ulcers.

Many of these granulomatous tumours occur in the region of the cæcum and may closely mimic a malignant tumour. Microscopically this granuloma resembles a mass of granulomatous tissue and consists of the same cellular elements, including Langhans' giant cells containing crystalline bodies (Rankin, F. W., Barga, J. A., and Buie, L. A., 1935, "The Colon, Rectum and Anus", p. 207, Philadelphia and London).

(3) *Phlegmonous enteritis*, originally described by Rokitsansky (1842), has the same pathology as that of Crohn's disease as pointed out by Clark and Wright (1937). Its resemblance to phlegmonous gastritis has already been commented upon.

(4) *Dysentery*.—Felsen (1936) claimed from a correlated study of 553 cases that both acute and chronic ileitis might result and that this pointed to a common ætiology. He claimed to have obtained positive cultures of *B. dysenteriæ*, Flexner and Sonne, during the acute stages and positive agglutination tests in the chronic. There has been no confirmation from other sources.

(5) *Sarcoidosis of Boeck*.—Williams and Nickerson first suggested that chronic ileitis might be related to sarcoidosis. With this object in view they emulsified a skin lesion from a proven case of sarcoidosis which gave positive intradermal reactions in two other cases of sarcoidosis and also in two of regional ileitis.

Sarcoidosis is identical with benign lymphogranulomatosis first described by Schaumann in 1914 (Hadfield, G., and Garrod, L. P., 1942, "Recent Advances in Pathology", p. 46, London). The histological picture (as in Crohn's disease) consists of large pale-staining cells of the endothelial type arranged in follicles resembling miliary tubercles as in some of them there is a centrally or laterally placed giant cell of the Langhans' type. I would like to suggest for future investigation that the virus which produces these lesions might be related to that of lymphogranuloma inguinale (which also gives rise to a similar cell picture). The difficulty surely consists in isolating this virus from intestinal and contaminated lesions. Ravant, Levaditi, Lambling, and Cachera (1932, *Bull. Acad. Méd., Paris*, 107, 3, 97) overcame this successfully in the case of lymphogranuloma inguinale by inserting a portion of the rectal stricture under the skin of guinea-pigs, subsequently dissecting out the enlarged lymphatic glands which contained the virus in a pure state, making an emulsion of them, and injecting this intracerebrally into white mice and monkeys, thus producing the typical encephalitis. In this manner the virus was isolated and transmitted in a pure state.

(6) *Lymphatic obstruction*.—Reichert and Mathes (1936), by injecting various sclerosing agents into the mesenteries and subserosal lymphatic channels and at the same time introducing bacteria intravenously, were able to produce œdema and extensive infiltration of the bowel wall. They concluded that regional ileitis was none other than a low-grade lymphatic infection, but Barrington-Ward and Norrish (1938, *Brit. J. Surg.*, 25, 530) suggested that disease of the mesenteric glands might be primary and that the ileitis might be due to the lymphatic block.

(7) *Infection through the mucosa*.—Although attempts have been made to identify organisms by aerobic and anaerobic cultures there are few reports of successful results.

account was given at the beginning of the last century by Combe and Saunders before the Royal College of Physicians, London, under the title of: "A singular case of stricture and thickening of the ileum."

Since 1932 a great literature has been built up around this disease. Approximately 160 papers dealing with this condition are listed in the *Cumulative Index* during the years 1939-1943. Shapiro, reviewing the literature in August 1939, tabulated 519 cases of regional ileitis in whom operative measures had been carried out (*Amer. J. med. Sci.*, 198, 269).

Regional ileitis usually and mainly affects the terminal portions of the ileum; it sometimes also extends to the jejunum and ileocaecal region. There is some evidence that circumscribed granulomata (so far known as non-specific granuloma) in the colon are of the same nature, as will be detailed later.

The regional lymphatic glands are enlarged and there is also thickening of the mesentery. Up to 1934 almost all recorded cases were to be found in the American literature, but since then there have been numerous references in English medical journals. The disease is more common in males and in Crohn's original series there were more than twice as many males as females. Originally described as affecting chiefly young adolescents, cases have been reported involving all ages.

The best and most recent account of the pathology is by A. Lyall (1945, *Glasgow med. J.*, 25, 1).

Pathology.—Two or more areas of the bowel may be rarely involved. The lengths of uninvolved bowel separating these areas are often called "skip areas". Blackburn and his co-workers (1939, *Bari's Hosp. Rep.*, 72, 181) speak of a "specific response" which they observed in 13 out of 20 cases. They noted marked hyperplasia of the lymphadenoid tissue in the submucosa producing cellular masses measuring 3 mm. in diameter; in some of these follicles the so-called "specific response" was seen and the germinal centres were replaced by proliferating endothelial cells. A basic problem which arises in the study of the pathology is whether this condition is chronic like tuberculosis or whether the early stages correspond to those of phlegmonous gastritis to which it bears some resemblance. As will be readily realized emphasis is laid on the histology as suggesting the identity of these various lesions.

The pathology can be divided into various stages:

(a) *Stage of acute suppuration.*—The affected length of the bowel is dark red in colour, greatly thickened and there are usually yellow shreds of fibrin adherent to the inner mucosa. The near-by glands are enlarged and red in colour. There is free, sometimes turbid, fluid in the peritoneal cavity. Miliary abscesses sometimes found in the submucosa resemble those seen in full-blown phlegmonous gastritis.

(b) *Chronic stage.*—Descriptions of this stage are commonly found in the literature. The naked-eye appearance of the affected bowel is typical and corresponds to Dalziel's simile of "an eel in a state of rigor mortis" or more commonly referred to as the "hose-pipe appearance". The serous surface of the bowel has a greyish-pink colour with white thickened patches representing organized fibrin. The terminal portions of the affected loop are often affixed to the pelvic brim by recent adhesions.

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Section for the Study of Disease in Children

President—Professor NORMAN B. CAPON, M.D.

[November 23, 1945]

Pulmonary Haemosiderosis.—A. D. BARLOW, M.B., M.R.C.P. (for Dr. DONALD PATERSON).

E. B., female, aged 6 years 10 months. Born 2.1.39.

Family history.—Mother alive and well. Father died of coronary thrombosis. Only child.*History.*—Normal birth; birth-weight 6 lb. 8 oz. Artificially fed. Born in Germany. Father German, mother Jewess.

Came to England at 8 months. Good health until 18 months, when she had a severe attack of bronchitis requiring admission to hospital. A chest X-ray had the appearance of military tuberculosis. At the age of 2 years attacks of breathlessness occurred every few weeks, diagnosed as asthma. At 3 years these attacks became less severe, being very mild at 3 years 6 months. An attack was characterized by severe cough and dyspnoea, but there was no sputum.

From 3½ years old she has always been very pale, her Hb. ranging from 30% to 70%. In December 1944 (aged 5½) and again in February 1945 she required blood transfusions.

Since January 1945 she has received liver injections (Examen 1 c.c. two to three times a week), iron and vitamin B (Benerva compound), but her Hb. has always remained below 70%.

In September 1945 she became rapidly more anæmic, and on 19.9.45 she was admitted to Great Ormond Street Hospital.

On admission.—She was very pale; weight 34 lb., nutrition poor. Liver 1 in. below costal margin. Spleen just palpable. Tonsillar glands enlarged, but no generalized glandular enlargement.

R.E.C.	2,800,000	White cells	8,600
Hb.	30% (4.2 grammes)	Lymphocytes	30%
C.I	0.55	Polymorphs:	
Reticulocytes	1.6%	Segmented	46%
No spherocytosis.		Stab	20%
Erythrocyte fragility normal.		Eosinophils	4%

Chest X-ray: A fine mottled appearance spreads almost to the periphery.

She was transfused, but during the following three weeks her red blood-count fell from 5.1 to 3.1 millions.

There was no evidence of bleeding: Occult blood negative; urine normal; no hæmoptysis at that time.

25.9.45.—Sternal puncture showed normal bone-marrow.

Total nucleated cell-count 86,000 per c.mm.

Hæmocyto blasts	0	Blast cells	0
Primary erythroblasts	1.5%	Myelocytes:	
Late erythroblasts	2%	Neutrophil	13%
Normoblasts	24%	Eosinophil	1%
		Metamyelocytes (neutrophil)	2%
		Polymorphs:	
		Segmented	7%
		Stab	34%
		Eosinophils	1.5%
Undifferentiated cells	0.25%	Lymphocytes:	
Mitotic cells	0.25%	Large	0.5%
		Small	13%

Leuko-erythroblastic ratio 2.7 : 1

Reticulocytes 5% (in peripheral blood)

Serum bilirubin 2.1 mg. per 100 c.c.

The evidence points to a hæmolytic process but not acholuric jaundice, as the fragility was normal, and no spherocytes were seen.

Mixer (1935, *Ann. Surg.*, 102, 674) and Jackman (1934, *Brit. J. Surg.*, 22, 27) indeed isolated a streptococcus of the enterogenous type from the floor of the ulcers as well as from the peritoneal fluid.

If the bacterial nature of the disease is accepted we must also be prepared to explain the mode of entry of the infection. The ulceration might well prove the site of entry of the primary infection. Ralphs suggested that an important part might be played by trauma such as fish bones.

Histology.—The best account of the histology is that of Hadfield, G. (1939, *Lancet* (ii), 775). This remains at present the only safe means of identifying the lesion and is, in fact, the result of hyperplasia of the lympho-reticular tissue leading to obstructive lymphœdema. The lymphadenoid masses vary in size, the largest forming cellular aggregates 3-4 mm. in diameter, visible to the naked eye. The smallest are 0.4 mm. in diameter and microscopic in size. In three-quarters of the cases these cellular nodes are scattered evenly through the œdematous mucosa, being 8-18 to the square centimetre. They show considerable cellular activity, a characteristic cellular response in a variable number of germinal centres making up a nodule of lymphadenoid tissue. The affected germinal centre is later replaced by proliferating endothelial cells with weakly staining nuclei.

In the midst of the cells constituting endothelial aggregates it is usually possible to find a Langhans' giant cell which, when mature, resembles the giant-cell system of miliary tuberculosis, but when this system has reached its full development all proliferation apparently ceases.

Never has the slightest evidence of caseation been seen. Some of the cells contain crystalline masses of various shapes and sizes. Probably the most arresting histological feature is the presence in the regional lymph nodes of a clear-cut specific formation of giant-cell systems identical with that of the thickened mucosa. The natural retrogression of this lesion can best be studied in this situation.

When viewed as an isolated and static histological picture the giant-cell systems, both in the glands and the bowel, are indistinguishable from those of tuberculosis, but the absence of caseation and of acid-fast bacilli force one to doubt its tubercular origin.

From the purely histological aspect, the appearance, evolution and retrogression, the giant-cell system of Crohn's disease more resembles the tissue reaction of Boeck's sarcoidosis than of tubercle infection.

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In view of the uniformly bad prognosis of the cases previously published, and in the hope that it might be possible to avert further hæmolytic episodes, her spleen was removed (by Mr. Charles Donald) on 19.10.45. However, the blood-count has again fallen since the operation, and once more there is evidence that a hæmolytic process is responsible.

Reticulocytes 10%, serum bilirubin 1.9 mg., urobilin in urine greater than normal.

Comment.—The evidence in favour of this being a case of pulmonary hæmosiderosis is: (1) The chest X-ray, persistent for five years; (2) the refractory anæmia; (3) biopsy of her lung, by aspiration (performed elsewhere), showed numerous hæmosiderin-filled macrophages; (4) a history of hæmoptysis.

Since discharge this child has had two small hæmoptyses.

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Refractory Anæmia.—A. D. BARLOW, M.B., M.R.C.P. (for Dr. DONALD PATERSON).

E. J. B., female. Normal birth (28.3.45). Weight 10 lb. 6 oz. No neonatal jaundice.

Family history.—Parents alive and well. Brother and sister normal (no neonatal jaundice or anæmia).

History.—Pallor gradually increased since birth, at 3 months her hæmoglobin was 24%. She was transfused, but three weeks later was again anæmic, the Hb. being 49%. Transfusion has been necessary every three to five weeks since then, six times in all. At 3 months old she passed bright red blood with her motions on one occasion, but has not had macroscopic blood since then. A purulent discharge from her right ear was noticed at 4 months.

Clinical findings.—Admitted to Great Ormond Street Hospital 29.9.45 aged 6 months. Well-nourished rather fat baby, weight 16 lb. Very pale, slight icteric tint to sclerotics. Liver 1 in., spleen 1½ in. below costal margin. Right ear discharging. Otherwise no abnormal findings, no general glandular enlargement.

Investigations.

30.9.45.—Blood-count:

R.B.C.	1,330,000	White cells	17,700 per c.mm.
Hb.	30% (4.2 grammes)	Lymphocytes	54%
C.I.	1.1	Polymorphs:	
Reticulocytes	0.2%	Segmented	10%
M.C.D.	7.1 μ	Stab	34%
Normoblasts	2 per 100 white cells	Eosinophils	2%
Hæmogram	9.11.45 (thirty-eight days after 500 c.c. Rh negative blood):		
R.B.C.	2,210,000	W.B.C.	10,500
Hb.	50% Sahli (7 grammes)	Polymorphs:	
C.I.	1.13	Segmented	15%
		Stab	13%
Normoblasts	2 per 100 W.B.C.	Eosinophils	2%
		Lymphocytes	69%
Slight anisocytosis and poikilocytosis		Monocytes	1%
No polychromasia			
		Platelets	350,000 per c.mm.
Reticulocytes	0.2%		
Packed cell vol.	20 c.c. per 100 c.c. (normal 42 c.c. per 100 c.c.)		
Mean corpuscular vol.	91 μ^3 (78 - 94 μ^3)		
Volume index	1.08 (0.85 - 1.15)		
Mean corpuscular Hb. concentration	35.5% (32 - 38%)		
Mean corpuscular diameter	7.1 μ		
B.S.R. (Wintrobe):			
Uncorrected	68 mm. per hour.		
Corrected for anæmia	19 mm. per hour.		
Red cell fragility	within normal limits.		

Bone-marrow (14.11.45) from tibia—400 cells counted.

Hæmocytoblasts	0	Leukoblasts	0.25%
Primary erythroblasts	1%	Myelocytes:	
Late erythroblasts	2.5%	Neutrophil	1%
Polychromatic normoblasts	10%	Eosinophil	0.25%
Hæmoglobinized normoblasts	7%	Metamyelocytes:	
		Neutrophil	1.75%
Large lymphocytes	2%	Eosinophil	0.25%
Small lymphocytes	53%	Polymorphs:	
		Neutrophil	9%
Mitotic cells	0.5%	Eosinophil	1%
Megakaryocytes	0.5%	Stab forms	10%

Leuko-erythroblastic ratio = 4:1

Total nucleated cells 37,000 per c.mm.

Mother group 0 Rh positive.

Baby group 0 Rh positive.

Baby's blood contains cold agglutinins in titre 1:4. W.R. and Kahn negative.

Blood cholesterol 95 mg. per 100 c.c.

Fractional test meal (histamine): Hypochlorhydria.

X-rays of chest, skull and long bones show no abnormality.

Progress.—Transfusion raised her red count to 4.86 millions; 100% Hb. But during the ensuing five weeks it gradually sank to 2.2 millions with 50% Hb. (7 grammes), resisting numerous forms of therapy.

The cause of her anæmia remains obscure: but amongst the possibilities which might be considered are:

Hæmorrhage: There was hæmorrhage from the bowel on one occasion, at 3 months. While in hospital her anæmia has increased steadily without any evidence of bleeding (the occult blood was weakly positive once, but repeatedly negative at other times).

Hæmolysis: Her serum bilirubin has been 2.5 mg. per 100 c.c., which may indicate increased hæmolysis (liver function, phosphatase and Takata-Ara tests normal), alternatively it may represent a defect in utilizing the products of normal erythrocyte destruction.

Diminished erythropoiesis: The persistently low reticulocyte count, the low total count of nucleated cells in the bone-marrow (37,000) with leuko-erythroblastic ratio of 4:1, considered in relation to the degree of anæmia (2.2 millions), would seem to indicate a low rate of formation of red cells.

Depression of the marrow by infection seems to be excluded by lack of improvement following mastoidectomy (no other focus of sepsis than her ear could be found).

She has not responded to large doses of iron (15 grains per day) by mouth, nor to liver by mouth or injection, nor to vitamin-B complex injections.

Nephrocalcinosis associated with Hyperchloræmia.—W. W. PAYNE, M.B., M.R.C.P.

G. F., female, aged 10½ years.

History.—Apparently normal till 1 year 8 months. Then "kidney trouble" for two years. Has had measles, scarlet fever, diphtheria and tonsillectomy. No relevant family history.

On examination.—Small, thin, intelligent child with knock knees. Good appetite. Polyuria. Height 43 in. Weight 43½ lb.

Investigations.—Urine alkaline, Sp.gr. 1006. Albumin 55 mg. per 100 c.c. Deposit: "Addis count" R.B.C. 8,000,000 per day. W.B.C. 220,000,000 per day. No casts or crystals. Urea concentration test: 9 a.m. 198 c.c. urea 0.81%; 10 a.m. 103 c.c. urea 1.20%; 11 a.m. 98 c.c. urea 1.25%; 12 noon 73 c.c. urea 1.24%.

X-ray (Dr. L. B. Blair): Multiple deposits of calcium density in both kidneys. Bones show some thinning of the cortex. No other abnormality.

Blood Investigations.

Hb. 75%, W.B.C. 8,900 per c.mm. (polys 36%; lymphos: large 4%, small 58%; eosinos. 2%).

	Before treatment	After treatment	Normal
Urea	22	27	20-35 mg. per 100 c.c.
Inorganic phosphorus	3.1	4.1	4-5.5 mg. per 100 c.c.
Calcium	10.2	-	9-11 mg. per 100 c.c.
Chlorides (as NaCl)	677	655	560-630 mg. per 100 c.c.
Bicarbonate	37	49	49-63 vols. CO ₂
Phosphatase	30.6	14	5-15 units
Cholesterol	169	-	100-200 mg. per 100 c.c.

Treatment (Albright *et al.*) 60 c.c. daily of the following solution: citric acid 140 grammes, sodium citrate 98 grammes, water to 1,000 ml. Also 30,000 units daily of vit. D.

This case resembles the cases described by Albright *et al.* [1], Baines *et al.* [2] and Rule and Grollman [3]. The cause is obscure.

My thanks are due to Dr. D. Paterson for permission to report this case.

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Two Cases of Banti's Syndrome: Hepatomegaly with Anæmia.—CHARLES PINCKNEY, F.R.C.P.

Two children of the same family, R. P. and K. P.

(1) R. P., female, aged 8. Admitted July 1944 with hæmatemesis.

Blood-count.—Before transfusion: R.B.C. 2,340,000; Hb. 39%; C.I. 0.8. W.B.C. 1,400 per c.mm. Leucocytes normal in appearance. Red cells: anisocytosis and polychromasia. Volume of packed cells: 19%. Mean corpuscular vol. 81 cu. μ . M.C. Hb. conc. 28%. M.C. diameter 7.6 μ , average thickness 1.8 μ . E.S.R. 20 mm. in one hour. Reticulocytes 8%.

After transfusion: Hb. 50%.

Given intravenous blood transfusion, 1 pint. Fragility curve normal. W.R. and Kahn negative. Serum bilirubin 0.4 mg. %, phosphatase 11 units, and colloidal gold reaction, weakly positive (1+). Urine—bile salts, urobilin, urobilinogen, bilirubin not detected. Sternal puncture—moderately active marrow with no significant changes. Stercobilin within normal limits. Galactose tolerance test—galactose index = 65 (normal).

(Mother's blood normal. W.R. and Kahn negative.)

Discharged with Hb. 83%.

Readmitted December 1944 with further hæmatemesis. Hb. 55%. Given further intravenous blood transfusion. Discharged with Hb. 72%.

Readmitted July 1945 with acute nephritis following acute tonsillitis. Made a good recovery in six weeks.

Liver function tests: Serum bilirubin 0.4 mg. per 100 ml. Thymol test 3 units. Serum colloidal gold weakly positive (1+). Urine urobilin negative.

Clinical examination shows liver enlarged three fingerbreadths below costal margin, hard, irregular, not tender. Spleen not enlarged.

(2) K. P., aged 3 years.

3.10.44: R.B.C. 4.65 millions; Hb. 84%; C.I. 0.9. W.B.C. 13,450 (polys. 59%, lymphos. 30%, monos. 11%). Red cells normal.

31.10.44: R.B.C. 4.96 millions; Hb. 87%; C.I. 0.90.

5.12.44: R.B.C. 4.89 millions; Hb. 86%; C.I. 0.89. W.B.C. 10,800 (polys. 24%, lymphos. 70%, monos. 3%, eosinos. 3%).

1.6.45: R.B.C. 5.37 millions; Hb. 96%; C.I. 0.9.

Clinical examination.—Abdomen: Liver enlarged three to four fingerbreadths below costal margin, hard, irregular and not tender. Spleen not enlarged.

Collapsed Intervertebral Discs following Lumbar Puncture.—URSULA JAMES, M.B., M.R.C.P.

Brian C., aged 4½ years, underwent lumbar puncture in January 1945 during investigation of recent fits. Fluid, which was withdrawn only after several attempts, was normal. No further fits.

One week later admitted to hospital. T. 104°F. Had been listless for three days, walking cautiously, hips flexed, supporting himself with hands above knees. He had been screaming at night and had vomited twice. He resented examination, especially flexion of hips, and sat up with difficulty. Lumbar spine rigid, loss of lordosis. He awakened frequently from sleep screaming with pain. C.S.F. normal. W.B.C. 15,150 (polys. 87.5%). Mantoux 1:1,000 and 1:100 negative. X-ray of spine normal.

Temperature settled for a few days then started to swing—child developed chicken-pox. Nine days later X-ray of spine showed narrowing of intervertebral space between L3 and L4. Narrowing increased and space L4 to L5 became affected. Four weeks later there was erosion of upper surface of fourth lumbar vertebra and sclerosis surrounded it.

After the first positive X-ray the child was put into a plaster bed in moderate extension. Penicillin was given for six days (50,000 units daily) because at this time it was thought that the lesion might be a low-grade osteomyelitis. The temperature fell and the general condition improved slowly.

He was kept in a plaster bed for four months, then walked about in a plaster jacket for two months. He was then and is still free from symptoms.

Two Cases of Ehlers-Danlos Syndrome.—F. L. KING-LEWIS, M.R.C.S., L.R.C.P., D.C.H.

(1) T. M., boy aged $3\frac{1}{2}$ years. Weight $27\frac{1}{4}$ lb.

History.—"When he falls, he does not cut himself, he just tears open." Bruises very easily.

Signs.—Looseness and over-elasticity of skin. Hyperextensibility of joints, especially fingers. Numerous scars, forehead, legs, &c. Scars have a papyraceous, "cigarette-paper" appearance and light violet colouring. Small pseudo-tumours of connective tissue in some of the scars. Facial appearance shows exaggeration of the inner canthus.

Investigations.—W.R. negative. Bleeding time five and a half minutes. Clotting time four minutes. Platelet count 250,000 per c.mm. Capillary resistance test normal. X-ray of tooth buds appears normal.

Family history.—No other cases known of congenital loose skin or hyper-extensible joints in the family. No consanguinity of parents.

(2) R. C., girl aged 9 years. Weight $51\frac{1}{2}$ lb.

History.—Cuts herself and bruises very easily.

Signs.—Looseness and hyperelasticity of skin, mainly over knees and elbow-joints. Hyperextensibility of joints. Can touch the back of her head with her heels. Scars, especially left knee and elbows, violet, "cigarette-paper" or papyraceous atrophic scars. Fatty nodule on left thumb and in scars on knee. Scars on knee completely anæsthetic. On 4.75×2 sq. in. of skin were resected and seven stitches inserted without any pain being experienced. Facial appearance shows some increase of the inner canthus.

Investigations.—Bleeding time four and a half minutes. Clotting time three minutes. Platelets normal. Capillary resistance test normal.

Family history.—Nothing relevant.

Trigeminal Nævus and Homolateral Intracranial Angioma associated with Hypertelorism.

—R. W. B. ELLIS, O.B.E., M.D.

John R., a boy aged 3 years 3 months, was born at full term by difficult breech delivery requiring forceps. He was said to have had a "fractured skull" following delivery. He is an only child and the parents are well and unrelated. The father has been examined and shows a mild degree of hypertelorism, and judging by photographs, one brother and one sister of the father are more markedly affected. No familial history of mental defect.

Convulsions first occurred at the age of 6 weeks, and epileptiform attacks have continued since that time. The child has been free for two to three months at a time, but whilst he has been under observation at Guy's Hospital (since June 1945) the fits have been frequent and entirely uncontrolled by drugs (luminal, sodium nitrate, bromides, epanutin). He has twice been admitted to hospital and found to have frequent auricular extrasystoles, pulsus bigeminus having been observed repeatedly. During his present admission (November 10 to 21, 1945) he has had twelve fits, each of short duration (one to one and a half minutes) and preceded by an aura. The attacks which have been observed usually start with throwing out of the left arm followed by upward deviation of the eyes, twitching of the right side of the face, and kicking or flexion of the right leg. (The mother, however, states that the left side is usually most affected.) It is doubtful if he actually loses consciousness in every attack. Recovery is very rapid, after which he complains of headache and usually wishes to pass urine. There has been no incontinence during the attack. On each occasion the pulse has been noted as being "slow and irregular", "missing beats", or pulsus bigeminus has been observed.

There has been no mental deterioration.

Physical examination.—Normal physical and mental development for age. There is a faint but well-defined facial nævus covering the greater part of the area of distribution of the ophthalmic division of the fifth nerve on the left. There is a moderate degree of hypertelorism, and facial asymmetry, with facial hypotrophy on the right. Eye movements normal. Discs and fundi normal. Between the attacks the limbs show normal tone and movement; the tendon reflexes are present and equal. Plantar reflexes flexor. No ataxia or nystagmus.

The area of cardiac dullness and the heart sounds are normal, but frequent extrasystoles or continued pulsus bigeminus are usually present.

Mantoux test (1:1,000) negative.

Lumbar puncture (15.11.45): Normal cerebrospinal fluid under normal pressure. W.R. and Lange negative.

Radiological report (Dr. T. Hills).—Skull: There is some asymmetry of the lesser wings of the sphenoid, but no evidence of fracture. There are a few small calcified areas on the left side, probably anterior to the central sulcus and situated rather deeply. Some irregularity of the floor of the sella.

Comment.—The association of a facial naevus, homolateral intracranial calcification, and epilepsy appears to justify the diagnosis of an intracranial angioma, although the history of birth injury introduces a confusing factor. The epilepsy in this case is not clearly focal, but it is probably significant that twitching of the right side only of the face has been observed in several attacks. There is also hypotrophy of the right side of the face. This contralateral hypotrophy has been described by Parkes Weber (1922)



Trigeminal naevus (left frontal region) with right-sided hypotrophy of face and hypertelorism.

in a patient also showing a left-sided intracranial lesion of this type, but here there was also a congenital spastic hemiplegia on the right. The naevus in the child shown is fainter than those in many of the published cases, but conforms to the almost invariable distribution, i.e. involving the greater part of the area of distribution of the ophthalmic division of the fifth nerve. It is exceptional to find calcification appearing at the site of the intracranial angioma at such an early age. In two cases of the same type (Ellis, 1931-2), no calcification was seen radiologically in the younger boy aged 1 year 9 months, whilst the older boy, aged 9 years, showed the classical "festooned" appearance (Parkes Weber—Dimitri's syndrome) within the skull. In all three cases the epilepsy proved completely resistant to medical treatment; in the eldest boy there was some mental retardation.

In this case, the association of hypertelorism is probably fortuitous. Hypertelorism is a heredo-familial condition, and although it has only been possible to examine the father it is almost certain (from the description and photographs) that one sister and one brother of the father are also affected. As in the family described by Abernethy (1927), there is no family history of associated mental defect.

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Section of Psychiatry

President—G. W. B. JAMES, C.B.E., M.C., M.D., D.P.M.

[November 13, 1945]

DISCUSSION: FORWARD PSYCHIATRY IN THE ARMY

Lieut.-Colonel Harold Palmer, R.A.M.C., opened the discussion by referring briefly to the history of the development of forward psychiatry. In France, prior to the Dunkirk campaign, he had been called upon to solve problems of storage psychiatry. From Dunkirk to El Alamein he had been associated with the development of methods of dealing with sick individuals. In Tripoli in 1943, the forward medical authorities of the 8th Army were persuaded to jettison the whole concept of psychiatric hospital treatment, to establish in its place a filtration centre serving three grades of rehabilitation centre and to initiate an "on the spot" system of re-allocation. In principle this meant dealing with the whole problem of the psychiatric and neurotic casualty as a problem of social medicine; as a result of this the whole set-up had only required 100 beds and two psychiatrists for an Army of 200,000 men, and was successful in returning 98% of the men to full duty. As far as possible these principles had been applied in Italy, but for one reason or another required modification, but the concept of the rehabilitation centre was carried on later in the U.K. in relation to many of the Normandy casualties.

In general, he felt that the chief lesson of his war experiences, as applied to civilian life, was the urgent and imperative need for creating filtration and rehabilitation centres in this country. In the sphere of treatment, narcosis and abreaction techniques have established themselves securely, but he felt that the latter would require patient evaluation in expert hands, otherwise it would fall into disrepute. The value of mechanized set-ups was not to be disregarded, and had their value in safeguarding the individual psychiatrist from fatigue. In particular he considered an insulin unit should always be available when handling psychotics, and he felt that the failure of many civilian authorities to provide such facilities was deplorable.

He suggested that the psychiatric problem would in all circumstances be found to be capable of analysis into six separate processes: Collection; filtration; treatment; rehabilitation; re-allocation; disposal; and he pointed out the dangers of assuming that all psychiatrists were equally equipped by experience or temperament to perform all these tasks with success.

Major C. Kenton, R.A.M.C.: Forward psychiatry in the Army includes in its scope the consideration of, and the methods of dealing with, the problems affecting the mental health and morale of troops that are exposed, by reason of geographical propinquity, to actual, or closely threatened, enemy action. This view brings into focus the prophylactic as well as the therapeutic aspects of the subject while, at the same time, it limits consideration to the problems of soldiers fighting in an ill-defined and fluctuating, but nevertheless recognizable, area of military operations. Rarely elsewhere in the Army have group loyalties and group sanctions operated so intensely, or so profoundly, affected the military psychiatric outlook.

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The prophylactic aspect of forward psychiatry may be briefly reviewed. Much can be done in this sphere by measures taken long before the entry of troops into the fighting area. I refer to adequate selection and screening, sound and intelligent training, promotion of good war purposiveness, good leadership, and the maintenance of efficient welfare for the troops. In the forward area these measures need to be continued, the Corps psychiatrist keeping himself informed of the changing problems, and advising on the steps to be taken to promote good morale and mental health, and the development of that degree of mental toughness essential in fighting troops. In addition he disseminates knowledge to regimental medical officers (and combatant officers) as to the causes and methods of psychiatric breakdown, how to check the incidence of such casualties, and how best to manage them when they do occur. The R.M.O. in helping to achieve these ends, acts as an integral part of the unit, and the close co-operation of the C.O. and company commanders is essential in the exercise of this good influence.

Notwithstanding the vigilance of those concerned with the prophylaxis against psychiatric breakdown, and how active and successful they are in the promotion of positive mental health and morale, it is still axiomatic that wherever fighting is in progress casualties of a psychiatric nature will occur, and that when the fighting is severe, the number of these casualties becomes such as to constitute a military problem. 10% to 15% of all living battle casualties are estimated to be psychiatric, and this figure is probably an understatement of the true position.

The military problem arising from this type of battle casualty resolves itself into: (a) preventing psychiatric casualties from impeding (i) actual fighting operations, (ii) the evacuation and treatment of the wounded; (b) selection and treatment of that proportion of men from the stream of psychiatric casualties who will be capable of early return to further effective fighting; (c) the prevention of deterioration in those unable to return early, or at all, to further fighting duty; (d) the factor of long-term conservation of man-power.

The therapeutic aim of forward psychiatry is to handle this military problem effectively in its early phase, and the methods adopted may now be discussed. The R.M.O., who first sees the psychiatric casualties, may, in very mild cases, send them back to their Company, after exhibiting a judicious mixture of firmness, sympathy, and friendly encouragement adapted to the individual case, and determined by his previous knowledge of the temperament and background of the individual soldiers under his medical charge. The decision to evacuate a case or to return him to duty is made by the R.M.O. acting as an integral part of his unit, and he is therefore guided by other factors in addition to the type and degree of psychiatric disturbance present. Some of these factors are: The military needs of the Unit at the moment; whether the soldier is still of some immediate use; the length of time the battle has been on; the state of morale in the Unit at the time; and the interests of the individual soldier.

If the decision to evacuate is taken, the diagnosis made is the purely "administrative" one of "exhaustion", and some notes from the platoon or company commander as to the circumstances of the breakdown are included, under sealed cover, with the field medical card. To all who are tremulous, apprehensive or agitated, a sedative such as Tab. Phenobarb. grain one or two is given. The sedation is continued at either the A.D.S. or M.D.S. in which the patient is staged *en route* for the Corps Exhaustion Centre. Phenobarb. grain one, three times daily is usually sufficient to keep the patient fairly quiet, relieve some of his distress, diminish the chance of his panicking, and prevent fixation of symptoms and further deterioration.

All those evacuated from the line with the diagnosis of "exhaustion" are speedily directed to a Corps exhaustion centre, which is usually a section of a specially selected field ambulance or C.C.S., and has a fluctuating number of beds. In this collecting centre major triage (or filtration) of the cases is undertaken, immediately after the essential needs of the soldier—a hot meal, a clean up of his usually dirty state, and attention to his bowels—have been fulfilled. This triage is based on a psychiatric interview in which a largely intuitive appraisal is made as to whether the soldier will soon be able to fight again or not. No definite criteria which help the psychiatrist in arriving at this judgment can be formulated easily, but the multitude of small component impressions obtained during the interview by an experienced Corps psychiatrist arouses the intuitive feeling of conviction that a soldier will or will not shortly be able to function effectively under conditions productive of great fear. In all those cases in which it is considered there is no reasonable probability of return to fighting duty within about five days, further sedative is administered, and they are evacuated to the advanced psychiatric centre. The diagnosis of "exhaustion" is abandoned and one which fits as nearly as possible into the nomenclature of diseases is made for each case. This is no easy matter

at times, particularly when otherwise normal soldiers of low "anxiety threshold" or low "anxiety tolerance" which renders them ineffective as combatants, need to be labelled with a psychiatric disorder to ensure their evacuation from the forward zone and their subsequent, more adequate, placement.

All those cases in which a reasonable probability of early return to fighting duty exists are retained for treatment at the Corps exhaustion centre. The principles underlying this treatment consist of: (a) continuation of, or increase in, sedation where indicated; (b) maintenance of military, rather than hospital patient, type of discipline; (c) continued contact with fellow-soldiers of the same or neighbouring fighting units; (d) some bolstering up of ego and morale; (e) maintenance of a curative atmosphere, so that early return to duty is expected by each soldier under treatment. Not all the cases retained at the centre prove fit to return to duty in the prescribed period, and these require to be evacuated to the advanced psychiatric centre. Figures of the proportion of cases admitted to the Corps exhaustion centre that can be returned to early fighting duty vary from Corps to Corps in the same and different theatres of war, and in the same Corps in varying conditions of warfare. The average proportion is rather less than 30%, the remaining 70% being evacuated to the advanced psychiatric centre. One of the major difficulties in this triage and treatment at the Corps exhaustion centre is that at the time of great operational activity, cases arrive at such a rate at the centre that the staff are rushed unduly and the optimum level of time for treatment often cannot be made available. This results in evacuation of some cases that would otherwise be unnecessary and unwise. In my opinion the Corps exhaustion centre is not the place for abreactive therapy, however tempting it may be in some cases. Such cases usually require much further psychotherapy and are best evacuated immediately to the advanced psychiatric centre without initiating any of the treatment other than continuation of sedation.

In the advanced psychiatric centre, therapy is less standardized and more definitely individual, although the patient is not regarded as completely detached from the group to which he has his loyalties and which imposes its sanctions upon him. A fairly high proportion of the cases are already improving and presenting a diminishing degree of psychiatric disability on admission to the centre. Treatment of these cases consists in appropriate instances, of rest, mild sedation with paraldehyde or barbiturates, alone or in combination, and one or two psychiatric interviews which have both a therapeutic and appraising function. Some cases are given insulin and glucose and extra diet to make up the loss of weight where this has occurred. A few cases, where the evidence of exhaustion is still apparent, are subjected to continuous narcosis of variable duration—sommifaine with paraldehyde supplement or the paraldehyde-phenobarbitone combination being the drugs we commonly used. A carefully worked out programme of occupational and diversional therapy, physical training, group activities of the leaderless type, and entertainment is made available for the patients, and they respond so well, even eagerly, to such a regime, that compulsion is almost never necessary. Within a period of ten to fourteen days this group of cases are discharged from the Centre, their destination depending on the appraisal by the psychiatrist as to (a) their probable effectiveness as fighting troops in the immediate future or (b) failing this, whether they need temporary or more permanent jobs not involving actual combat activities. Approximately 10% of the admissions to the centre come into the first category, and these cases are sent to the Army rehabilitation centre—which is not a medical unit—for a short period of military training and toughening prior to return to fighting duty. Those in the second category are despatched to a reallocation centre where they are interviewed and tested by personnel selection staff to determine their aptitudes and abilities with a view to satisfactory placement within the theatre. The majority of these cases in the second category are usually medically regraded, as a necessary precaution to prevent their too precipitate use as fighting troops.

The more severe cases require a therapeutic programme of greater complexity for their treatment and rehabilitation. Fortunately they form a minority of the case-load in the advanced psychiatric centre. Severe anxiety states, particularly when associated with mutism, stupor and other regressive manifestations, and amnesic states are treated by abreactive methods in the first place. I consider sodium pentothal as the most valuable agent for this purpose. The shorter induction period and less prolonged duration of effect of this drug are advantages as compared with sodium amytal. The technique, apart from slow intravenous injection ceasing just before actual sleep is produced, is varied in each individual case, the aim being the release of the emotions connected with the traumatic experiences. Whether these experiences are re-enacted or merely recalled, or whether they are not entirely factual but have an admixture of phantasy, is not very material, as long as suitable, repressed emotion related to these experiences is released, and the more or less overwhelmed ego can resume its functions. I prefer to release this emotion in one sitting, but my American colleagues favoured such release in controlled quantities. The response to abreactive therapy in severe battle-precipitated neuroses is usually dramatic and spectacular; but, in effect, ego control is still weak, although beginning to function. Strengthening of this control is aided by a direct, necessarily brief, psychotherapy, utilizing transference and explanatory techniques. Occasionally convulsive shock therapy succeeds where psychotherapy fails. Concurrently with this psychotherapy, the ancillary methods of occupational therapy, physical rehabilitation, and group activities are all used. A fair proportion of the severe cases are rendered fit enough by these methods to be sent to the reallocation centre for placement in non-combatant jobs. Those that are not considered fit enough, together with psychotics

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at times, particularly when otherwise normal soldiers of low "anxiety threshold" or low "anxiety tolerance" which renders them ineffective as combatants, need to be labelled with a psychiatric disorder to ensure their evacuation from the forward zone and their subsequent, more adequate, placement.

All those cases in which a reasonable probability of early return to fighting duty exists are retained for treatment at the Corps exhaustion centre. The principles underlying this treatment consist of: (a) continuation of, or increase in, sedation where indicated; (b) maintenance of military, rather than hospital patient, type of discipline; (c) continued contact with fellow-soldiers of the same or neighbouring fighting units; (d) some bolstering up of ego and morale; (e) maintenance of a curative atmosphere, so that early return to duty is expected by each soldier under treatment. Not all the cases retained at the centre prove fit to return to duty in the prescribed period, and these require to be evacuated to the advanced psychiatric centre. Figures of the proportion of cases admitted to the Corps exhaustion centre that can be returned to early fighting duty vary from Corps to Corps in the same and different theatres of war, and in the same Corps in varying conditions of warfare. The average proportion is rather less than 30%, the remaining 70% being evacuated to the advanced psychiatric centre. One of the major difficulties in this triage and treatment at the Corps exhaustion centre is that at the time of great operational activity, cases arrive at such a rate at the centre that the staff are rushed unduly and the optimum level of time for treatment often cannot be made available. This results in evacuation of some cases that would otherwise be unnecessary and unwise. In my opinion the Corps exhaustion centre is not the place for abreactive therapy, however tempting it may be in some cases. Such cases usually require much further psychotherapy and are best evacuated immediately to the advanced psychiatric centre without initiating any of the treatment other than continuation of sedation.

In the advanced psychiatric centre, therapy is less standardized and more definitely individual, although the patient is not regarded as completely detached from the group to which he has his loyalties and which imposes its sanctions upon him. A fairly high proportion of the cases are already improving and presenting a diminishing degree of psychiatric disability on admission to the centre. Treatment of these cases consists in appropriate instances, of rest, mild sedation with paraldehyde or barbiturates, alone or in combination, and one or two psychiatric interviews which have both a therapeutic and appraising function. Some cases are given insulin and glucose and extra diet to make up the loss of weight where this has occurred. A few cases, where the evidence of exhaustion is still apparent, are subjected to continuous narcosis of variable duration—somniafine with paraldehyde supplement or the paraldehyde-phenobarbitone combination being the drugs we commonly used. A carefully worked out programme of occupational and diversional therapy, physical training, group activities of the leaderless type, and entertainment is made available for the patients, and they respond so well, even eagerly, to such a regime, that compulsion is almost never necessary. Within a period of ten to fourteen days this group of cases are discharged from the Centre, their destination depending on the appraisal by the psychiatrist as to (a) their probable effectiveness as fighting troops in the immediate future or (b) failing this, whether they need temporary or more permanent jobs not involving actual combat activities. Approximately 10% of the admissions to the centre come into the first category, and these cases are sent to the Army rehabilitation centre—which is not a medical unit—for a short period of military training and toughening prior to return to fighting duty. Those in the second category are despatched to a reallocation centre where they are interviewed and tested by personnel selection staff to determine their aptitudes and abilities with a view to satisfactory placement within the theatre. The majority of these cases in the second category are usually medically regraded, as a necessary precaution to prevent their too precipitate use as fighting troops.

The more severe cases require a therapeutic programme of greater complexity for their treatment and rehabilitation. Fortunately they form a minority of the case-load in the advanced psychiatric centre. Severe anxiety states, particularly when associated with mutism, stupor and other regressive manifestations, and amnesic states are treated by abreactive methods in the first place. I consider sodium pentothal as the most valuable agent for this purpose. The shorter induction period and less prolonged duration of effect of this drug are advantages as compared with sodium amytal. The technique, apart from slow intravenous injection ceasing just before actual sleep is produced, is varied in each individual case, the aim being the release of the emotions connected with the traumatic experiences. Whether these experiences are re-enacted or merely recalled, or whether they are not entirely factual but have an admixture of phantasy, is not very material, as long as suitable, repressed emotion related to these experiences is released, and the more or less overwhelmed ego can resume its functions. I prefer to release this emotion in one sitting, but my American colleagues favoured such release in controlled quantities. The response to abreactive therapy in severe battle-precipitated neuroses is usually dramatic and spectacular; but, in effect, ego control is still weak, although beginning to function. Strengthening of this control is aided by a direct, necessarily brief, psychotherapy, utilizing transference and explanatory techniques. Occasionally convulsive shock therapy succeeds where psychotherapy fails. Concurrently with this psychotherapy, the ancillary methods of occupational therapy, physical rehabilitation, and group activities are all used. A fair proportion of the severe cases are rendered fit enough by these methods to be sent to the reallocation centre for placement in non-combatant jobs. Those that are not considered fit enough, together with psychotics

and gross psychopaths, are evacuated to a rear (or base) psychiatric centre for long-term treatment or invaliding to the U.K. This group forms approximately 10% to 12% of the admissions to the advanced psychiatric centre, and their handling at the rear centre is outside the scope of the present subject.

From what I have said, it can be seen that at the separate organization levels, limited therapeutic goals are aimed at, varying with the different levels. Despite this stratification, I hope I have indicated the dynamic approach to the problem which is manifested by the psychiatrists in the field and their attempts to deal with the realities of the situation confronting them.

A brief reference may be made as to the results obtained by the methods of handling and treatment I have described. The figures for the N. African and Italian campaigns up to September 1944 for all cases where the disposal has been recorded, and including cases seen at all levels, show that of 22,454 patients 18,777 (83.6%) were retained for duty in the theatre of war and 3,677 (16.4%) were invalided home. Of those retained for duty in the theatre, no exact figure can be given for soldiers that were re-employed in active fighting duties, but it is in the region of 30% to 35%.

Lieut.-Colonel H. B. Craigie, R.A.M.C.: In view of the remarkable advances made in instruments of mutilation and destruction during the recent war, and of the extremes of mental and physical stress to which so many men were exposed, the percentage incidence of psychiatric breakdown was less than might have been expected. The numerical incidence, however, was sufficiently high to present a considerable problem; and much of it was avoidable, highly wasteful in its immediate effects, and potentially mischievous in its end-results.

In psychiatry as elsewhere, prevention is better than cure; and prevention, to be effective, depends upon an adequate understanding of the causes of psychiatric breakdown. In practice, there was rarely any single cause for breakdown in forward areas: the causative factors varied according to the individual himself, the group in which he functioned, and the environment by which he was surrounded.

A faulty personal history, a constitutional predisposition to neurosis, was the most important single factor in the causation of breakdown: if associated with a broken home life, or a faulty family history, the prognosis was so much the worse. "The qualities of a man that make him the best citizen", said Marshal Foch, "are those that make him the best soldier"; and this underlies the principles of personnel and officer selection employed in the Army since 1941. Men must be selected for service positively, not just because they have proved useless for anything else.

The individual's ultimate success or failure depended largely upon the group of which he became a member. High group morale depended upon proper training, upon knowledge of and devotion to the cause, upon adequate equipment, and upon inspired leadership. Good leadership, high morale, and a low psychiatric casualty rate were synonymous.

The environment provided the final test; and it was found that battle stress alone was neither the most common nor the most important cause of breakdown in forward areas; there was, in fact no fundamental difference between the causes of breakdown in forward and in base areas. Brigadier James said very aptly—"men break down for fear of life, not of death": and indirect mental or physical stresses were often much more significant in their effect upon the soldier than combat itself. Loss of sleep and physical exhaustion, persistent and overwhelming noise, thirst, hunger and dirt, physical ill-health, the inability to retaliate at the enemy, were associated factors of great importance. The factor of greatest and most universal application was the so-called "separation anxiety". Domestic separation was of the greatest importance to the average soldier; the longer in time, the further in space, the separation, the greater the anxiety.

Mental hygiene, the care of the mental health of the Army, proved during the war in many respects more important than physical hygiene; and its importance is at least equal in application to the community at peace. It is reasonable to assume that psychiatrists, in the light of the experience gained in these matters during war, may be able to make contributions of value to the solution of the very similar problems confronting us in the post-war years.

Lieut.-Colonel T. F. Main, R.A.M.C.: In the forward psychiatric centre, therapeutic practice should, one supposes, remain objective, illumined only by psychiatric knowledge. It would be nice to report that in the forward areas psychiatry is cool and accurate and unimpassioned. But if we take thought for an instant we can see that this can never be so. Psychiatric disease and normality are only relative matters affected by current social standards and culture patterns. An emotional state which might at home be

described legitimately as severe anxiety, might on the field be called bravery or cowardice depending on whether the psychiatrist himself is frightened or not.

A forceful moral diagnosis is therefore sometimes made by the psychiatrist before he applies the new nomenclature of the Royal College of Physicians, and treatment is sometimes affected by the psychiatrist's needs as well as by the patient's.

Other influences also affect objectivity. There is an understandable general desire during a war to feel important and useful. The inevitable hardships and sacrifices of war affect everyone to some extent, and lead to various emotional by-products of bitterness and impotence, anger, and—if one's own job is not heroic or important enough—to defensive swashbuckling or a guilt-driven compassion for the others who have to undertake risks of death in battle. Sentimentality and anger about neurotic soldiers, therefore, commonly influence clinical judgment in prognosis and disposal.

Now if the judgment of psychiatrists is liable to lack objectivity in the face of great world events, it must not surprise us if excessive emotions also arise in others. Violent attitudes in medical colleagues and superior officers are part of the total social setting within which the psychiatrist works and influence for better or worse his daily judgment and his over-all policy.

The mental health of a fighting force is not the same thing as the mental health of a nation at war. With the differing functions, different standards are needed. If a sergeant can recover his poise for one month, it can be regarded as a satisfactory therapeutic result in an Army fighting for its very life, though such a result would not be worth having in civilian life. Then the stresses which such a man must be capable of withstanding are very different from those which would operate upon him in civilian life—and they must be fully understood by the psychiatrist. Lastly, the positive factors which will support the mental health of such a man are different in the forward area from those in the rear areas. The job of the psychiatrist, in fact, demands a grasp of the social as well as the medical variants which influence treatment and disposal.

One campaign does not seem to train a psychiatrist automatically for another. In the Middle East the great separation from home, the flat barren wilderness in which the men lived, the poor food and water supply, the rarity of action, the occasional big battles dominated by the spandau, the 88 mm. and the mortar, lasting only a few days, contrast with the battles of the Normandy Bridgehead which went on without remission for over two months in familiar green fields and copses, with scarcity of sleep, the multi-barrelled mortar, and the continued carnage as the great stresses. In Burma, I am told, it was not the noise of explosions nor the power of enemy weapons that were the stresses, but silence in jungle patrols, the fear of being seen without seeing, the difficulty of sleeping with a calm mind, and the long separation from home.

Yet these stresses can be classified. The sense of separation from home, from its security and its comforting permanence and its familiar reassurance of one's personal status is a permanent stress. A camaraderie is the only human recompense for a threatening sense of impotence in the face of death and the waywardness of elemental forces and the decisions of the mighty who use soldiers like pawns.

The lonely homesick man, overwhelmed by insecurity, showing anxiety and hysterical illness, is met sometimes before he has even been in battle, together with the men who have carried out their social obligations in the face of fantastic dangers until their sense of security too has gone. There are others who have contained their anxiety, supported by comradeship and affection until the death of their friends has left them bereaved, to face further dangers alone. The man who has killed too much, the officer who has lost his men through an error of judgment, the tank commander who escaped alone from a burning tank—present pictures of guilt and depression that may be psychotic in depth. Fleeting schizophrenic screens may be drawn for a few days over anguish too gross to be borne.

These acute clinical pictures arise very often in conjunction with loss of sleep. While this can be a symptom it is often a necessary condition of some battles, and gross fatigue alone leads some men to the psychiatrist.

Acute cases repay the simple forward treatment of rest and sedation and justify the existence of forward psychiatric centres. The bonds which tie men to their fellows have not yet been broken, and some 30% to 60% can be returned fit to carry on. The numbers correlate indirectly with the surgical casualties—following about 3 days behind the curve of daily incidence. But it is not a parallel curve; as the surgical casualties rise, the psychiatric casualties rise out of all proportion. Depending on the type of battle, 2% to 30% of all casualties may be psychiatric.

When the numbers are high during a big battle, you may imagine the alarm in high places, the increase in diagnosis of "cowardice" by administrative staffs, and the reluctance to recognize the problem as a psychiatric one. At these times all the slack in senior super-egos is taken in, and some of the wrath falls of course on the patients and occasionally even on their therapist. That is in the day's work. One popular view at such times—popular in rear areas at least—is that access to the psychiatrist will discourage the fighting men who are sticking it out. This may be so, but I have yet to meet a regimental medical officer who knows of a single instance of a good man being discouraged by the knowledge that if he became a casualty of any sort he would get looked after.

The "chronic" cases seen in quiet periods are a mixed bag. Some of them are chronic neurotics, but many are men with persistent symptoms from earlier battles, particularly of guilt and depression about comrade-loss or with anxiety which has not resolved spontaneously after rest. The home worries, too, mount as a campaign goes on and become increasingly a source of military inefficiency. The prognosis with the cases that appear during quiet periods is not as good as with the acute cases, and hospital treatment and re-allocation are needed.

The forward psychiatrist has made himself a familiar figure in the war, and has proved his value in every theatre since 1940. He cannot work miracles, but by persistently plying his craft, keeping his head amid the shifting moral attitudes towards his patients, and remaining, in so far as his own situation allows, objective and unsentimental, honest about his failures and modest about his successes, he can serve the men of his formation in a way granted to few medical men. Such a result, however, is achieved not by heroics, but by good psychiatry.

[December 11, 1945]

DISCUSSION ON THE IMPORTANCE OF DIET IN MENTAL ILLNESS

Dr. W. Rees Thomas: For many years pellagra has occurred in this country, arising as occasional cases in the community and among patients in mental hospitals. In the early days, before the cause of pellagra was known, we described a dermatitis of the hands and face resulting from the administration of drugs such as sulphonamide and trional. We know now that this was pellagra and it arose not only from a deficient intake of vitamins of the B group, but also from a failure of the body mechanism to absorb it or, if absorbed, to use it for its proper purposes. To-day we know of occasional cases of pellagra arising in mental hospitals, though most of the cases reported were admitted suffering from the disease. I am not proposing, however, to deal with specific diseases arising from food deficiencies but with the more general relationship between health and food, and in particular its effect on patients undergoing treatment for mental illness. How far this may have an influence on accelerating or retarding recovery in mental illness is a matter which we could discuss without forming a definite conclusion. It can, however, be said that subnormal food must lead to subnormal health. The outstanding example is the effect of vitamin C on the healing of wounds, and I feel sure there would be general agreement that in the treatment of any form of mental illness a factor of importance is the quantity and relative sufficiency of the food; the caloric value is important for patients who are not confined to bed or who exhibit considerable physical activity as part of the illness.

Shortly after the outbreak of war in 1939 most of us discovered that we were losing weight. A similar phenomenon occurred in mental hospitals. The change was so obvious that in 1941 an investigation was made to determine whether gains and losses of weight differed from changes occurring in the same patients during the two years before the outbreak.

In seventeen hospitals the weight records between September 1937 and September 1941 were examined. The figures indicated that the loss of weight in the period 1939-41 had been very considerable and affected quite three-quarters of the patients who had been in the hospital during the whole period. This is not quite so bad as it sounds; the peacetime figures show that normally 45 to 50% of the patients tend to lose weight over a period of two years. This is a selected group consisting entirely of those whose illness is prolonged.

The hospitals were divided into two groups, depending on whether or not they were overcrowded. Comparison of the records of loss of weight showed that the degree of

overcrowding existing at the time made no difference to the proportion of patients who lost weight.

At a later date a further investigation was carried out by Dr. Nicole at the Winwick Mental Hospital. The results indicated that from 1942 onwards the position gave no cause for anxiety. The proportion losing weight had greatly diminished and did not differ widely from the figures for the period 1937-39. It is difficult to say just why this change took place but in 1942 we became more food conscious and everybody did a good deal to improve the variety, the quantity, and the balance of the diets, and hospitals were now able, without much trouble to themselves, to have the diets analysed and the quantity of vitamins and minerals estimated as a daily average over a period of one month.

I will now refer to the general food situation during the war up to 1943 as related in "Food Consumption Levels (1944)". The daily caloric value of the food supplied to the people of this country before the war was about 3,000. In 1939-41 there was a sharp fall in the meat, visible fats, sugar and fruit which greatly reduced the palatability, as well as the nutritional, value of food. At the period of greatest shortage in the first half of 1941 calories fell to 2,680 and it appears that there were indications that the diet was inadequate. In 1942 the figures showed an improvement and from then onwards have remained almost constant at a caloric value of about 2,800, though fats and animal proteins remain considerably below pre-war level. The importance of this for my present purpose is to indicate that in 1941 the food was not sufficient and in 1942 and onwards it can therefore have only been slightly above the level of sufficiency. These figures do not represent the actual intake of food but of food issued for consumption.

A comparison of these two events, that is the loss of weight and the standard of food issues, suggests that the reduction of food supplies showed itself in a loss of weight amongst the hospital population—at least that part of it represented by patients undergoing prolonged treatment. The recovery from 1942 onwards is parallel to a better food situation and a time of greater attention to the minerals and vitamins as well as the caloric value of the foods supplied. There are, however, many other factors to be taken into account, though none of them can easily account for the initial loss of weight to the end of 1941 and the subsequent recovery.

I go on now to consider the effect food may have on the death-rate in hospitals. We have lived through two great wars and an examination of the death-rates in hospitals during these periods may show that diet in one war affected the death-rate. The mean death-rate in mental hospitals for the five-year period 1910-14 was 96 per thousand, and the death-rate during the years 1915-21 given in the table below might be compared with this pre-war figure. The table also indicates similar data for the years around the war 1939-44.

TABLE I.—DEATHS PER THOUSAND.

	General population	Mental hospitals		General population	Mental hospitals
1910-14	13.8	96	1935-39	12.1	68.5
1915	15.7	121	1940	14.4	82.6
1916	14.3	126	1941	13.15	91.7
1917	14.2	176	1942	12.3	79.9
1918	17.3	203	1943	13.0	69.8
1919	14.0	129	1944	12.7	69.0
1920	12.4	87			
1921	12.1	84			

A comparison between the two sets of figures shows very marked differences. During the period 1915-18 there was a progressive rise in the mental hospital death-rate throughout.

The abrupt fall in the death-rate in 1919 and the further reduction in 1920 to a figure well below the 1910-14 rate shows that conditions improved rapidly after the war, and that within a year they were normal again.

During the recent war, the death-rate increased in 1941 to a rate which was 33% higher than the pre-war average, and thereafter slowly fell to a figure which in 1944 was only slightly above the rate for 1935-39, i.e. 69 compared with 68.5.

The figures for men and women are given separately in the second table; they show that for women the rate fell in 1943 to 64, which, excepting for the years 1930 (60.6) and 1938 (61.8), is the lowest ever recorded.

TABLE II.—PROPORTION PER CENT. OF DEATHS TO AVERAGE NUMBER RESIDENT.

	Male	Female	Total
1937	7.09	6.04	7.0
1938	6.82	6.18	6.47*
1939	7.05	6.86	7.21
1940	8.06	7.04	8.26
1941	10.46	8.21	9.17
1942	8.81	7.36	7.99
1943	7.74	6.40	6.98
1944	7.49	6.46	6.90

* Lowest ever recorded.

It is noteworthy that this occurred at a period when the shortage of female nurses was greater than at any time during the century.

If we consider for a moment the factors which might have affected the death-rates during these wars we find that during both periods there were certain common stresses and strains.

Overcrowding occurred in both periods in the early war years. In the first war, however, the death-rate was so high that overcrowding was much reduced in the later years. Black-out restrictions were much more severe in the recent war, resulting in a low standard of ventilation in dormitories and bedrooms.

Changes in the ages and types of patients admitted would be similar in both wars.

If shortage of staff had been an important factor in determining the death-rate it would have showed results on the women's side of our mental hospitals during the past three years. Though I am unable to quote exact figures for the period 1914-18 I am assured that at no time during the 1914-18 war was the staff shortage on the female side as acute as it has become during this period when so much woman-labour was diverted to factories producing munitions of war.

Enemy action and the disturbance to patients caused by "alerts" undoubtedly produced abnormal conditions, but we can agree that on the whole the stress during 1940-41, particularly in certain areas in the East and South, was greater than that caused by Zeppelin raids.

On the whole, then, it would seem that the stresses in the recent war were more severe, due to equal, if not greater, overcrowding, stricter black-out regulations, inferior ventilation at night, greater shortage of both male and female staff, and much mental and physical strain arising from enemy air action by night. The causes of the high death-rate in the 1914-18 period were the subject of an investigation by the Board of Control. They concluded that the unavoidable reduction in quantity and deterioration in quality of the food supplied to patients (especially in regard to flour) were the main factors in determining the increase in sickness and corresponding increase in death-rates among patients in institutions for the insane and defective; but that, had the diet been normal, there would still have been a considerable rise over pre-war rates due to other war conditions. The conditions referred to were the lower physical condition and greater age of patients admitted, the impairment of staff efficiency, transfer of patients from one mental hospital to another, and overcrowding combined with bad ventilation. I think it is reasonable to assume that the difference between the records in the two wars shows something of the advance in knowledge of food and feeding.

An analysis of the dietaries of some two-thirds of the hundred or so mental hospitals in this country was carried out during the recent war. Each hospital publishes an official dietary with menus running a three or four weeks' rota. We found that these dietaries gave an incorrect and exceptionally rosy picture of the situation; consequently the analysis was made on the basis of the actual issues of food to the kitchen, taken from the records in the weekly issue books in the stores department. There were certain difficulties in carrying out the analysis because the extra food given to certain patients known as "workers" had to be excluded from the general issue and naturally diet given to sick patients had to be left out of account. The number of working patients given extra food varied within wide limits; of the 83,000 patients concerned some 27% of them received an average caloric value of 290 per day as an extra. An additional 10% of the patients were in receipt either of sick diet or of some extra to ordinary diet. The remaining 63% received the ordinary diet with nothing extra: the mean caloric value of the ordinary diet was 2,360, ranging from 1,956 to 2,731 calories a day. Vitamin A was 2,110 international units, and vitamin C 85 mg. per person each day.

It is not easy to say what should be the caloric value of a diet issued to a group of adult patients many of whom are quite old and many physically as well as mentally ill.

The average figure of 2,360 indicates that the patients of about half the hospitals receive less than this amount. The present evidence indicates that the food is sufficient providing that the distribution between wards takes account of the type and activity of the patients in their classified groups.

In considering whether a diet is adequate we base our views on the relation of the quantities to standards which have been set up by the National Research Council of the U.S.A., which has approved a minimum standard applicable only to short term periods but which provides mineral and vitamin allowances approximately 70% of the ordinary standard. In 1943 a special committee of the Joint Food Board, as quoted in "Food Consumption Levels, 1944", thought that the diet in this country, with the exception perhaps of vitamin A and ascorbic acid, and possibly also of riboflavin and thiamin, was adequate to meet the intake requirements based on the full National Research Council standards. Diets in mental hospitals provide a sufficiency of calcium, iron and vitamins of the B group.

There is an important difference between the food issued to the general population and that supplied in a mental hospital. The maintenance of a satisfactory level of calories and vitamins in the United Kingdom diets has involved a substantial increase in the use of cereals and potatoes. In 1943 this contributed 43% of the total caloric supply compared with 34% before the war. For the mental hospital, however, the present figure is between 50% and 60% and consequently the supply of potatoes ensures, at least in the summer time, an adequate ration of ascorbic acid. Even throughout the winter months the supply of vitamin C has exceeded 58 mg. per head per day, largely through the use of leafy, yellow and green vegetables. As the losses during cooking and preparation are considerable the intake in winter would not exceed an average of 30 mg. of ascorbic acid.

The supply of vitamin A is obtained largely from fats, milk, growing vegetables, eggs, and carrots. The ordinary diet in most mental hospitals provides about half the supply from carrots, the remainder coming from miscellaneous items of food. The mean figure of 2,110 I.U. per day showed that in most hospitals the supply of vitamin A was below the optimum level. The deficiency can be made good by the use of about half a pound of carrots per patient per week. Carrot is not available in every week of the year, but as vitamin A is stored for considerable periods in the liver, irregularity of supply is not a matter of vital importance.

The average mental hospital has one advantage over the many other hospitals. There are farms from which the supply of milk for patients comes daily to the hospital. The quantity available for the ordinary diet has usually been ample, and in this respect they have been more fortunate than the general population.

The suggestion that diet can be maintained at a satisfactory level without great difficulty does not affect the much more difficult question of cooking and presentation. The common complaint is lack of variety and though we, as members of the population, complain of the same thing we do not suffer in the same degree. Repetition in the presentation of the same items of food makes food unpalatable and the patients' inability to take an occasional meal outside the hospital tends to lower appetite. All this leads to waste and a lowering of the caloric value of the food intake. The patient suffering from mental illness is often too busy to bother about food or too depressed to want it. Thus with a supply of food that is adequate though little above the minimum it behoves us in every case of mental illness to pay the closest attention to the details of presentation and variety as well as to the quantity and content of the food taken. Our scientists teach us that even in a time of plenty a diet cannot be taken for granted even when the patient makes no complaint.

Dr. H. E. Magee: The Ministry of Food is advised regarding diet for invalids by the Special Diets Committee of the Medical Research Council on which the Ministry of Health is represented. This Committee gives medical advice as to whether patients suffering from any particular disease should have special allowances of rationed or other foods. The various allowances for different types of invalids are set out in the special leaflet, Med. 2, which has been sent to every medical practitioner. The Committee has not recommended any special priorities for mental patients as such. Mental patients, suffering from non-mental complaints such as diabetes or tuberculosis, are entitled to the prescribed allowances of rationed or other foods. Mental hospitals, like all others, can also obtain a priority allowance of 2 lb. fish weekly for every patient requiring a "light

diet". Apart from this allowance of fish mental hospitals are rationed like an ordinary institution for healthy people.

The requirements of the individual mental patient will vary with the amount of muscular exercise he performs. If he is doing farm work daily in the open air he would require a diet providing about 3,500 calories or more daily, but if he is quiet and confined indoors he might only require 2,400 calories or less. Other things being equal the needs of mental patients vary with their complaints. The melancholic or paranoic type might require only about 2,000 calories a day or less, whereas the excitable type with exaggerated reflexes, lack of co-ordination, continual unrest and insomnia might well require 4,000 calories a day. If the demands of such a person are not fully met it would seem from general principles that he would tend to become more rather than less excitable, at any rate for a time. The experiences of most people during air raids, particularly the V.I. bombardment, supports this deduction. The severe mental and physical strain with few interruptions, which most normal people experienced, were unquestionably reduced by taking small snacks in between the ordinary meals. It will be recalled that the Radio Doctor at this time advised people to eat often and to be sure to eat enough. I have no doubt that very many people derived much comfort from this advice.

Balancing up the needs of the various patients in a given mental hospital it is probable that the average gross requirement for the adult male is round about 3,000 calories per head daily and for women probably about 2,200. Within this average there will of course be wide fluctuations, but the allowances of food permitted and the mode of serving should be sufficiently elastic to permit of these needs being fully supplied. If the diet includes all the rations and points foods and if bread, potatoes, oatmeal and fresh vegetables are given to satisfaction, there need be no fear of any deficiency whether in regard to energy, proteins, minerals or vitamins. Table I shows how a 3,000 calorie diet could be constructed from the rationed and unrationed foods. Rationed foods, providing a sensible choice is made of the points, will supply about 1,040 calories and about 30 grammes protein most of which is of animal origin. The remaining 2,000 calories would have to be made up mainly from bread and flour which provide about 1,100 calories, or more than one-third of the total day's needs, and from potatoes and oatmeal, each of which provide about 220 calories or about one-thirteenth of the day's needs. The remaining calories would have to come from things like sausages, fish, and offal, when they can be obtained.

The unrationed foods provide about 72 grammes of protein, over twice that provided by the rationed foods. Bread and flour alone give as much as 41 grammes daily, whereas rationed meat only provides seven. It is true that animal protein is of higher biological value than any kind of vegetable protein, but vegetable proteins are also valuable. It is stated from time to time that the requirements of animal protein are so many grammes daily. There is no experimental evidence which enables us to place the requirements of animal protein at a given figure. Indeed we cannot say that the human body *requires* (in an indispensable sense) animal protein, at any rate after the stage of childhood has passed. In childhood there is, of course, a definite requirement, but for adults, all we can say is that it is very desirable that a proportion, which we cannot define, of the total protein should be of animal origin.

We often hear complaints that certain people, particularly hospital patients and staff, are not getting enough protein, that their diets are too starchy and therefore unsuitable. If you consider Table I you will find that this cannot happen, provided the people are getting all or the bulk of their rationed foods and provided the total diet gives them sufficient calories. To obtain a diet of sufficient calories which would be at the same time too low in protein, would not be easy; indeed with present rations it would be impossible. The calories would have to come from bacon, fats, sugar, jam and vegetables and fruit. The first four of these would provide only about 500 calories a day, and vegetables and fruit could certainly not provide the rest. It can be taken as a broad general rule that if a person of ordinary tastes consumes sufficient calories from the foods available he can scarcely avoid having enough protein, minerals and vitamins. In fact, the wartime food policy was so planned as to make this possible.

Table II shows the standard intakes of nutrients recommended by the Commission on Nutrition of the League of Nations as applied to the population of Great Britain. I have only given the figures for the adult man and woman because it is with these that we are mainly concerned. The calorie level for the average man is 3,000 and the protein 70 grammes a day. This is much lower than the 101 grammes which can be obtained from a 3,000 calorie diet under present rations. There is another scale of st

requirements in considerable vogue to-day, namely, that of the National Research Council of the U.S.A. It was drawn up in 1941 by the Americans but it has not received international approval. In regard to calories, proteins and minerals it is not substantially different from the scale of the League of Nations, but the scale for vitamins is far in excess of that of the League of Nations. Take vitamin C as an example. The N.R.C. recommends for children 5 to 14 years 50 to 75 mg. of vitamin C daily. Bransby and Wagner (*Brit. med. J.*, 1945 (ii), 682) found by dietary surveys that 426 school children in

TABLE I.

Rationed Foods : Weekly Amounts

	Amount	Protein (grammes)	Calories
Milk, 2 pints	40 oz.	36.0	680
Dried milk	1 "	10.2	97
Bacon	3 "	8.4	330
Butter	3 "	0.3	633
Margarine	3 "	—	654
Cooking fat	2 "	—	506
Cheese	3 "	21.3	351
Meat : Beef	7 "	25.2	518
Mutton	7 "	21.7	546
Sugar	8 "	—	864
Preserves	4 "	0.4	284
Eggs	1 "	6.2	78
Dried eggs	0.63 oz.	8.2	103
Dried fruit	1 oz.	0.7	56
Breakfast cereals	8 "	28.0	776
Pilchards	5 "	22.5	285
Rice, &c.	4 "	7.2	396
Canned meats	2 "	8.6	142
Per day		29.3	1,044

Unrationed Foods : Weekly Amounts

Bread	84 oz.	201.6	5,880
Potatoes	84 "	33.6	1,344
Green veg.	20 "	12.0	100
Root veg.	20 "	4.0	100
Flour	20 "	68.0	1,960
Sausage	8 "	26.4	488
Liver	4 "	19.2	160
Cocoa	2 "	11.6	250
White fish	8 "	24.0	104
Fat fish	8 "	24.0	296
Oatmeal	16 "	54.4	1,776
Semolina	8 "	24.0	768
Per day		71.8	1,889

Rationed and Unrationed Foods : Daily

Total per day	101.1	2,933
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TABLE II.—STANDARDS FOR ADEQUATE DIET PER DAY.

	League of Nations Commission		National Research Council Moderately Active	
	Male	Female	Male	Female
Calories	21+	21+	21+	21+
Protein grammes	3,000	2,400	3,000	2,500
Calcium grammes	70	60	70	60
Iron mg.	0.8	0.8	0.8	0.8
Vitamin A I.U.	10	10	12	12
Vitamin B ₁ mg.	3,000	3,000	5,000	5,000
Vitamin C mg.	1	0.85	1.8	1.5
	30	30	75	70

Stoke-on-Trent and Salford were consuming for most of the year an average of about 20 to 25 mg. of vitamin C daily. The school meals were analysed for vitamin C and they were found to contain only from 2 to 19 mg. per meal. The school meal for many children is the main, if not the only, source of vitamin C. These children were very carefully examined 3 or 4 times during the course of the year but no evidence of any sort was found suggestive of deficiency of vitamin C. There is other and more convincing evidence not yet published indicating that the recommended allowances of vitamins A and C of the N.R.C. are far too high, at any rate for the inhabitants of this island.

One of the most striking things that have come to light from liberated Europe is that frank deficiency disease, particularly vitamin deficiency, has been rarely observed whatever the degree or duration of the shortage of food. Nutritional œdema, loss of weight, diarrhoea and more rarely anæmia have been observed at various times and in various places, but very rarely pellagra, beri-beri, night blindness or other well-defined deficiency condition. What have always been observed however, whatever the degree or duration

of the starvation, were progressive asthenia, apathy, listlessness, lack of attention to personal hygiene, indifference to personal or communal welfare, until finally the sufferers became almost indifferent to their fate.

Without the will to live the treatment of a diseased person is a very up-hill and, may be, an impossible task. Insufficient food tends to blunt the desire to live. Adequate feeding tends to restore and to sharpen it. Good feeding besides building up the diseased body also enables the mind, which controls the body, to function properly.

In conclusion here are some observations made in 1942-43 in the (male) mental hospital of St. Anne in Paris by Randoin (*Bull. Acad. Méd.*, 1943, 127, 559). Before the war the average calorie intake was about 2,877 daily and the death-rate 10%; in 1941-42 the average calorie intake was about 1,750 and the death-rate 21%. On this level of diet the patients lost up to 5 kg. per head in six months, but when in 1943 the diet was increased all round by about 25% most of the losses in weight were restored in six months. This interesting paper has only recently come to my notice.

Dr. S. W. Hardwick said that he was not complacent about the question of diet and mental disorder. He believed that mental disorders associated with vitamin deficiencies were by no means uncommon. He had described in 1943 12 cases of pellagra complicating chronic mental disease and most of these were seen by Professor Sydenstricker during his visit to this country. Dr. Hardwick had encountered additional cases of pellagra in his mental hospital since then. He said that when Professor Sydenstricker with Dr. Rees Thomas had only seen one case of pellagra during their visit to a certain mental hospital—this did not necessarily mean that there was only one pellagrin in the population of that hospital at that time. There may have been cases showing no overt signs of pellagra at that time.

No mention had been made of acute vitamin deficiency. This was disappointing because it seemed that here was a field where the interests of the dietetic expert and the psychiatrist intersected. He referred for example to acute nicotinic acid (niacin) deficiency, a condition which had been described by Sydenstricker and Cleckley, and others. There was evidence, in Dr. Hardwick's opinion, that niacin deficiency, probably secondary to dietetic deficiency, was an important causative factor in some cases of mental illness.

In conclusion Dr. Hardwick mentioned that he had been associated with Professor Ellinger of the Lister Institute and Mr. R. Benesch in certain problems arising from vitamin deficiency. A nicotinamide saturation test had been devised, and this might lead the way to simpler and quicker methods of biochemical diagnosis.

Section of Physical Medicine

President—J. W. T. PATTERSON, M.D., F.R.C.P.Ed.

[October 10, 1945]

Physical Medicine in the Army

Its Effect on Civil Practice. [Abstract]

PRESIDENT'S ADDRESS

By J. W. T. PATTERSON, M.D., F.R.C.P.Ed.

Late Lieut.-Colonel R.A.M.C., Late Assistant Director of Hygiene, War Office

THE post-war world, on whose threshold we stand to-day presents a very different picture from the one we knew before the war. New discoveries, new modes of thought and new social conditions challenge us on every side.

That challenge must be accepted and our first step is to take stock of where we stand. Only then may we determine what contribution Medicine, with its high traditions of service, can make in the changing world around us.

My contribution concerns itself with the development of Physical Medicine in the Army.

"Physical Medicine Specialists" in the Army started by advising on the individual rehabilitation of soldiers referred to military convalescent depots for retraining. Soon they were advising on "group" rehabilitation and then on the general progression of training within the depot.

Next came the study of rehabilitation methods *outside* the depot in order (a) to attempt to standardize the physical condition of men arriving at the depot from such variable sources as special chest hospitals, head injuries, general hospitals, orthopaedic hospitals and auxiliary hospitals; (b) to ensure that steady progression was maintained throughout from bedside, through initial convalescence, to convalescent depot and, at the other extreme, from convalescent depot to unit.

This latter necessitated a study of the relative demands made by varying employments in different units and a study of the training of the fit. This liaison with training authorities resulted in Physical Medicine giving advice on training and drawing up physical standards for the selection of special troops, e.g. parachutists, frogmen, &c.

Physical Medicine played an important part in the medical aspects of selection not only for the special troops but for the less fit personnel and was responsible for much of the spade work entailed in introducing the new system of Army Medical Classification which is to be a feature of the peacetime Army.

Physical Medicine, with the invaluable assistance of the Army Physical Training Corps, was responsible for the success of the physical development centres where thousands of recruits likely to break down under routine training were able to "make the grade" as A 1 personnel after special preliminary training.

Physical Medicine made considerable contributions to the large-scale investigation of various important problems relative to health and training and the study of the sub-standard recruit.

Such was the unfolding of the opportunities presented to Physical Medicine in the Army.

What may we say of the lessons we have learned from these experiences?

(1) That successful rehabilitation depends on a thorough co-ordination of all remedial measures from the bedside, through ambulatory convalescence, right up to final reinstatement.

(2) That reduction in the period of convalescence is just as important as the reduction in the duration of hospitalization. The latter has been brought home to the profession through the shortage of hospital accommodation. The former is equally important from the point of view of industry and from that of the patients' economic circumstances.

(3) That the medical profession must be prepared to study and disseminate knowledge in what are the most effective measures for rapid and complete restoration after disability and must be prepared to condemn all personal idiosyncrasies in regard to methods which are proved to be wasteful and less than fully effective.

(4) That successful rehabilitation demands a thorough knowledge of *all* the operations involved in the employment for which the individual is being prepared.

(5) That successful rehabilitation involves the rehabilitation of the *whole man*, psychological and social as well as physical.

(6) That the medical profession must be made to realize the importance of job analysis. It should busy itself with the investigation of job analysis from a medical point of view so that, among other considerations, its rehabilitation work shall be more purposeful and more scientific.

(7) That Medicine must be prepared to advise on the capacity in which a permanently disabled person may be most adequately and suitably employed.

(8) That Medicine must be brought to realize the importance of physical education and its interest and supervision enlisted in this highly effective factor in the maintenance and achievement of physical efficiency.

(9) That Medicine must be prepared to extend its preventive aspect more completely. It must investigate and adjudicate on all measures likely to improve and maintain health in addition to concentrating on established disease processes. Such a preventive outlook demands investigation of the so-called Normal, seeking to establish those ranges of normality, outside which preventive measures must be undertaken to avoid ultimate disability.

[Meeting held on March 14, 1945, at St. Thomas's Hospital, London. Continued from August issue of "Proceedings"]

The Use of X-rays in the Treatment of Indurations due to Scars and Chronic Inflammation

By R. D. S. RHYS-LEWIS, M.B., B.Chir., D.M.R.

A NUMBER of cases have been treated in this hospital with X-rays in conjunction with surgery and physical treatment. They showed persistent induration and scar formation following acute infections, and the object of treatment has been to hasten resolution of the induration and to restore the function of the affected part.

The ages of the patients treated ranged from 4 to 69 years, the majority being in the third and fourth decades. There was in all cases a history of an injury which had become septic, and in nearly all the injuries had occurred on the extremities. The tendon-sheaths had often been involved. Half the lesions were caused by penetrating wounds from enemy shells and bombs, the remainder occurred as a result of the hazards of industrial and everyday life.

The patients were referred for treatment from two to six months after the original injury, and had already been given surgical and physical treatment including the sulphonamides and penicillin. They fell into two main groups: (1) Chronic induration of the soft tissues following acute infection. (2) Thickened plaques of keloid scar-tissue often with deep attachment and limitation of movement.

The X-ray treatment of each type of case differs in many respects.

Treatment of Chronic Infections

When the acute stage of an infection of the soft tissues has settled down, there is often an indurated area where resolution is delayed. This can usually be successfully treated with X-rays where surgery, physical treatment and chemotherapy have failed, and the induration rapidly made to disappear.

Several theories have been put forward to explain the action of X-rays on inflammatory conditions.

It is probable that the effect of irradiation is not on the causative organism or agent, but on the morbid anatomical process produced in the tissues. Most authorities are agreed that the infiltrating leucocytes are very sensitive to X-rays and readily break down with the liberation of enzymes. In a focus of chronic inflammation the capillaries and tissue spaces are blocked by lymphocytes, which can be eliminated by a very small dose of X-rays and the blood supply correspondingly improved. The capillaries themselves dilate as a result of the direct action of the X-rays and a local passive hyperemia is thus produced.

There is a further view held by many authorities that non-specific antibodies are produced in the tissues which are subjected to irradiation.

The doses used are so small that the risk of damage to normal tissues is minimal.

Technique.—In the treatment of these cases, filtered X-rays of medium penetration generated at medium kilo-voltage are suitable. The field irradiated is sufficient, amply to cover the indurated area, and the dose given is small. We use here 50-100 r every four to five days. The number of treatments varies with the speed of resolution, but seldom are more than four or five treatments necessary.

There are no general constitutional effects on the patient and there should be no skin reaction. The induration usually resolves completely; the inconvenience is very slight as each attendance is only a matter of minutes.

The Treatment of Scars

These cases were mainly thickened scars following recent injuries or surgical intervention for complicated and infected wounds.

These scars showed keloid formation on the surface with firm induration deep to the scar composed of actively dividing cells and deep keloid formation.

The irradiation of such scars is followed after an interval of time by pallor and flattening of the surface keloid with softening of the underlying thickening and a resultant increase in mobility and restoration of the function of the affected part.

It might be mentioned that the irradiation of old contracted fibrous scars is not only useless, but unwise. They are very resistant to the action of X-rays, and high doses given in an attempt to influence them only result in an increase in fibrosis due to the action of the X-rays themselves or even in tissue damage and breakdown in the form of radionecrosis.

Technique.—The technique of irradiation of these scars has been evolved by many workers for both radium and X-rays, and with the advent of more satisfactory apparatus in recent years and careful physical calibration, it has been possible to work out an accurate form of treatment.

Between 1930 and 1942 much experimental and clinical work was done by Levitt and Gillies and the effects of increasing doses were studied. It was found that the best results were obtained by a very nice adjustment of the dosage, as evidenced by the biological effect of the production of a mild erythema of the scar. Such a reaction is necessary to produce the optimum result.

The field irradiated is confined to the scar, and, here, we have used filtered X-rays generated at potentials varying from 60 to 200 kV., according to the degree of penetration and quality of ray required. The usual kV. employed was 140, except where deep structures had to be avoided, when X-rays generated at a lower potential 60 kV. were preferred.

The dosage has been administered either as a single high dose to a small area or in fractionated doses if the area involved was large, or where it was desired to avoid constitutional effects on the patient, especially when high-voltage X-rays were employed.

A single dose of 500-800 r according to the site and size of field was given for all voltages, or 1,500-2,000 r in fractionated doses over periods varying from five to twenty-two days. No standardized "routine" treatment was thought advisable as the cases varied considerably in many respects and each was treated according to its merits.

In none of our cases has this treatment been repeated.

Contra-indications and Dangers of this Form of Therapy

In the treatment of indurations following infection, where small doses are used at intervals of several days, the risks attendant upon X-ray therapy are not very great. But in the treatment of thickened scars, where high dosage is used and medium and high-voltage X-rays often employed, there are many factors to be thought of.

The age and general condition of the patient must be taken into account. In the young, the injuries are often on the extremities and it must be remembered that the growing ends of bones underlying the scar area to be irradiated can be irreparably damaged by X-rays with resultant deformity such as brachydactyly. It is in such lesions that rays of low penetrating power are indicated.

Scars occurring in the neighbourhood of the secreting glands or the globe of the eye must be treated in such a way that damage does not occur to these structures.

The possibility of depilation of hair and eyebrows must be borne in mind when scars occur on the scalp or forehead.

So-called "Contact" therapy—that is low-voltage X-rays delivered at short focus skin distance—should always be employed in the treatment of abdominal scars in the female to avoid damage to the ovaries which might occur with more penetrating rays.

The use of other radiations such as U.V.L. to the areas where X-ray therapy is contemplated should be suspended, and the exposure of the part to strong summer sunlight should also be avoided.

Lastly it is important to consider the soil in which the lesion may be found, as the presence of arteriosclerosis, syphilis, diabetes or a poor blood supply due to damage to the main artery to the part affected may have impaired the tolerance of the tissues to the action of X-rays.

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[November 14, 1945]

DISCUSSION ON THE CLINICAL IMPLICATIONS OF THE
DISABLED PERSONS (EMPLOYMENT) ACT, 1944

Dr. Harold Balme (*Medical Officer in charge of Rehabilitation, Ministry of Health*).—The Disabled Persons (Employment) Act, which came into law eighteen months ago, has not yet received the attention which it merits from the medical profession, and, so far as I know, this is the first occasion on which its clinical implications have been discussed by an official medical organization. And yet it will be obvious, from a study of the Act, that its provisions raise large issues in which the medical profession as a whole and the hospital services of the country in particular will be directly involved.

In general terms, the purposes of the Act may be summarized as follows:

First, it establishes the important principle that disability of any shape or form—whether congenital or acquired, medical or surgical, general or local—constitutes a claim upon the State for assistance, and that such assistance should not merely be expressed in terms of financial allowances or pensions, but rather in measures calculated to restore physical function, wherever possible, and reinstate the disabled person in some suitable form of gainful occupation.

Secondly, it makes provision for the vocational training and industrial resettlement of those who, subsequent to hospital treatment for injury or sickness, need to learn a new profession, trade or occupation before being fit to resume employment.

Thirdly, it assists disabled persons to secure work by means of a requirement on employers to engage a stated proportion of men or women so handicapped.

Fourthly, it provides employment under sheltered conditions for those who are severely disabled, but are able to do regular paid work provided that they do not have to stand up to the working conditions of competitive employment.

Such a programme may appear at first sight to constitute an industrial problem rather than a medical one, and to be more particularly concerned with the organization of suitable training courses and the finding of suitable jobs for the man or woman who, in the words of the Act, is "substantially handicapped in obtaining or keeping employment, or in undertaking work on his own account of a kind which, apart from that injury, disease or deformity, would be suited to his age, experience and qualifications". But it would be quite a mistake to regard this as being primarily an industrial question, for the ultimate success of this important measure of social legislation depends, in certain vital respects, on the active co-operation of the health services of this country, without which the real purpose of the Act will be frustrated. It is the purpose of this paper to suggest some of the lines along which such co-operation will be required, and to indicate means by which it can be effectively provided.

In the first place it will be noted that under the terms of the Act a Register is to be compiled of all persons substantially handicapped by reason of disability and whose disability is likely to last for a period of not less than six months, only children under working age and patients spending their whole time in hospitals or sanatoria being excluded from the list. This Register has already been opened, and it is estimated that by the time it is completed it will contain no less than a million to a million and a half names of people who will have the right to claim assistance in rehabilitation and industrial resettlement. The man with a spinal injury who can no longer work at the coal face in a stooping position; the patient with recurrent dermatitis of industrial origin; the man or woman who cannot stand excessive noise, or glare, or a dusty atmosphere; the man with limited movements of particular joints, or weakness of special muscular groups; the deaf and blind and limbless; the man with chronic peptic ulcer, who can only do regular work when hours are steady and opportunities for suitable diet available; and the chronic neurotic with his many varieties of psychosomatic disturbance—all of these, and many other groups, will qualify for admission to the Register. It is obvious, therefore, that it will be in the interests of all concerned—employers, employment exchanges and taxpayers alike—that their numbers should be kept to an irreducible minimum. This Register will not only be a record of disabled persons for whom suitable jobs must, if possible, be found; it will also be a register of the failure of our hospital services to prevent residual disability. It is obvious that in a large number of cases it is quite impossible to prevent such an end-result—we can hardly be held accountable for the congenital disabilities, at any rate!—but the health services of the future will be expected to do everything which lies in their power to limit the number of those who are left with disabilities which form a substantial handicap to the prosecution of their work.

In the second place, no scheme of vocational training, or of successful placement of disabled persons in industry, can ever succeed without medical guidance, particularly from those who actually treated the patients during their period of severe sickness or injury, and are able to assess the end-result in terms of loss of functional capacity. It is only by such assessment, expressed in terms that are easily interpreted by those upon whom will fall the task of finding new jobs or providing vocational training courses, that such disabled persons can be satisfactorily settled in fresh employment.

Thirdly, there will be need of very careful follow-up work and periodical review, in order to ascertain at the earliest possible moment if disabled persons are unable to stand up to the physical or psychological strain of the work which they have been advised to attempt, and require a further course of medical treatment or a transfer to some less strenuous form of occupation.

The particular directions, therefore, in which medical assistance is essential to the successful operation of this Act, may be summed up in the phrases: Prevention of residual disability; assessment of loss of functional capacity; and periodic follow-up and review. Let us now see how such assistance could be afforded, and what demands will be made on our future hospital and health services to provide the necessary facilities for medical rehabilitation, vocational guidance, and resettlement in suitable forms of industrial occupation.

MEDICAL REHABILITATION

The prevention of physical disability after severe accident or illness, by means of active forms of physiotherapy under expert guidance, has long been advocated by all experts in physical medicine, but it is only during this recent war that practical measures have been adopted, on any wide scale, to give expression to this purpose. The war has fostered the cause of medical rehabilitation in more ways than one. It has provided an overriding motive, in view of the urgent importance of getting Service men and women and essential war workers back to duty with as much speed and with as little residual disability as possible. It has made possible the erection and equipment of suitable rehabilitation departments in a large number of Service and E.M.S. Hospitals, and the appointment of the necessary staff of physiotherapists, physical training instructors and occupational therapists. And it has ensured the retention of patients in hospital or convalescent depot throughout the convalescent stage—at any rate, in the case of Service patients—thus making it possible to continue active measures of physical rehabilitation until the fullest measure of functional restoration has been obtained.

This development of rehabilitation facilities has not been confined to Service hospitals or to those special institutions which were taken over and up-graded by the E.M.S. for the reception of Service cases and air-raid casualties. It has since spread to a number of peacetime voluntary and local authority hospitals; at the present time there are approximately 350 civilian hospitals in the country, including those temporarily used by the E.M.S., which have established rehabilitation departments in greater or less degree. This encouraging result has been brought about by means of the special survey of rehabilitation facilities, organized by the E.M.S. in 1942 and carried out by experts in nearly 500 hospitals; the recommendations forwarded to hospital authorities arising from that survey; the special courses in rehabilitation technique organized and financed by the Ministry of Health at selected rehabilitation centres, and already attended by 254 doctors and 420 physiotherapists from 322 hospitals; and the practical assistance afforded to hospitals in the shape of equipment, gymnastic and sports apparatus, and improvised buildings.

The special conditions pertaining to wartime hospital practice, and the type of personnel which formed the majority of the patients for whom active rehabilitation has been provided, have necessarily been influential factors in shaping the programme of rehabilitation adopted at the most successful hospital centres, and many of these conditions will no longer exist in civilian hospital practice. Certain well-established principles have, however, emerged from this experience which should be of the greatest value in laying plans for the development of hospital rehabilitation as an integral part of our future health services and these may be summarized as follows:

(1) *Continuity of medical supervision.*—Rehabilitation is not to be regarded as something secondary to medical and surgical treatment, commenced and carried out during the period of convalescence. It is an essential part of treatment itself, and should therefore be prescribed by the physician or surgeon in charge of the case, who should maintain close supervision of the patient's progress both in the in-patient wards and out-patient department, and also, wherever possible, at the residential rehabilitation centre to which

the more severely disabled must be transferred for the final stages of their physical reconditioning, as described later in this paper.

(2) *Range of medical and surgical disabilities suitable for active rehabilitation.*—There is an unfortunate impression, widely prevalent, that active rehabilitation is only applicable to orthopaedic disabilities and traumatic surgery. This misapprehension largely derives from the historical fact that modern methods of physical rehabilitation sprang into popularity with the successful and brilliant work of Robert Jones and his orthopaedic colleagues during the war of 1914-18, and that the B.M.A. Committee on Fractures and the Delevingne Commission confined their recommendations to the setting up of rehabilitation departments in connexion with fracture clinics and the treatment of persons injured by accidents. The experience of this present war has proved that rehabilitation should not, and must not, be confined within such narrow limits, and that the same principles apply equally to all forms of medical and surgical disability or loss of physical and psychological function, resulting from prolonged immobilization or severe illness. Encouraging results have already been obtained by the scientific application of these principles to a variety of chest complaints, including chronic bronchitis and emphysema, asthma, pneumonia, empyema, and the after-treatment of lobectomy, pneumonectomy and thoracoplasty; to the recovery of abdominal muscular tone and the prevention of liability to hernia or prolapse after laparotomy or childbirth; to the rapid and complete recovery of the mobility of the fingers and hands after septic infections and burns; to the treatment of certain forms of arthritis which have reached a chronic stage, with a normal blood sedimentation rate; to the psychological readjustment of patients suffering from various manifestations of psychoneurosis; and to the partial or complete restoration of function after injury or disease of the central nervous system. In this last connexion, the brilliant results which have been obtained at Stoke Mandeville, in the treatment of spinal paraplegics under Dr. Guttmann's leadership, have proved convincingly that even so apparently hopeless a case as the patient with destruction of the spinal cord, and with complete loss of function of bladder and rectum and lower limbs, can yet be got on to his feet and enabled to take up useful forms of gainful occupation, as the result of a scientifically devised programme of thorough rehabilitation and vocational training.

(3) *Appointment of trained staff.*—The provision of an adequate hospital rehabilitation service in a hospital is not a matter which can be safely left to the haphazard device of any physiotherapist who happens to have been practising massage and electrotherapy there over a course of years. It is essentially a scientific form of treatment which is constantly changing and improving its technique, and can only be properly entrusted to a trained staff, thoroughly conversant with modern methods. At the head of such a staff there should obviously be, wherever possible, a specialist in physical medicine, to whom the actual superintendence of all forms of rehabilitation treatment should be delegated by the physician or surgeon in charge of the case, and who should have a free hand in ordering the particular forms of physiotherapy, physical exercises and occupational handicrafts best suited to each patient. In hospitals which have no physical medicine expert on the staff this duty is often entrusted to an orthopaedist, a surgeon in charge of the fracture clinic, or a resident medical or surgical officer, but it is an important principle, which war experience has abundantly confirmed, that this function should always be discharged by a single medical officer, who should be responsible for the training and general supervision of the various ancillary workers, and who should do everything possible to weld them into a united team.

Regular conferences on the problems presented by various types of disability, and the particular part which physiotherapy, group exercises, remedial games and occupational therapy severally play at each stage of recovery, are an important means of educating and uniting such a team, and should constitute one of the duties of such a rehabilitation medical officer.

(4) *A balanced and progressive programme.*—If rehabilitation is to be carried out scientifically and efficiently, it is essential that a carefully thought-out programme should be laid down for each type of medical and surgical disability and for each successive grade in the process of recovery. The basic principles underlying such a programme are fundamentally the same, whatever be the nature of the disability, combining as they do the use of physiotherapy and active exercises, remedial games and appropriate occupational handicrafts, alternating with prescribed periods of rest, relaxation and mental entertainment. The actual programme for each patient must, however, always be an individual matter, and must be related, not only to his particular illness or injury, but also to the type of work which he normally follows and to which he hopes to return. In the case of heavy manual workers, with reasonable expectation of being sufficiently restored to be able to resume their former occupation, it is obvious that the programme of rehabilita-

tion must be gradually stepped up, by means of strenuous exercises and heavy occupational handicrafts, until the patient is able to stand a muscular strain comparable to what he undergoes at work.

The initial stages of rehabilitation necessarily take place in the wards and out-patient department, for it cannot be too often emphasized that rehabilitation is not merely planned convalescence, as it is sometimes called, but is an integral part of medical and surgical treatment, and should commence as early as possible after the onset of illness or accident. All rehabilitation medical officers are agreed that their best results are obtained in cases which have been under supervision from the day of admission, and which have followed an appropriate programme from the first day on which it can be safely prescribed. It is the quadriceps and hamstrings drill given before and after cartilage operations, or after fractures of the lower limbs; the early abdominal exercises after laparotomy or childbirth; the early movements of fingers and hands after injuries and infections; and the special lower-thoracic and diaphragmatic breathing exercises given both before and after operation in the case of thoracic and upper abdominal surgery, which make for speedy recovery and help to prevent residual disability.

The later stages of rehabilitation, on the other hand, are best carried out, if possible, away from the hospital atmosphere. In the case of the more serious forms of disability, there is no question that the ideal method is by transfer to a residential rehabilitation centre, linked to the transferring hospital, so as to provide that continuity of medical supervision to which reference has already been made, but provided with ample facilities in the form of good playing fields, gymnasium, swimming pool and opportunity for the heavier handicrafts. For the minor forms of disability, every effort should be made to provide for the later stages of rehabilitation to be carried out in industry itself, and in those industrial concerns where a special rehabilitation workshop has been established—as at the Austin Motor Works, Vauxhall Motors, &c.—such patients are put on to the type of work which will provide the regular exercising of the particular muscle groups which are weak or the joints which are stiff, under the supervision of the industrial medical officer. In this way not only is the period of hospitalization materially shortened, but the patient has the added stimulus of being back on a money-earning job.

The important points which must be borne in mind in the preparation of a programme of rehabilitation, either in the early or late stages, are (a) that it must be well balanced; (b) that it must provide ample time for complete rest and relaxation; (c) that it must be progressive, increasing in content and in strenuousness as the patient begins to recover physical and mental vigour; (d) that it must provide for mental exercise and recreation, as well as physical; and (e) that it must always be related to the kind of work to which the patient hopes to return.

(5) *The care of the psychological factor.*—The experience which has been gained during the war at the special neurosis centres set up by the Service departments and by the E.M.S., and the valuable experimental work carried out at Roffey Park, have clearly proved the value of physical reconditioning, selected occupational handicrafts and group games as adjuncts to expert psychiatric treatment for patients suffering from psychoneurotic disorders. Apart, however, from patients in whom some definite form of neurosis is manifested, there is an element of psychological disturbance present in a great many cases of physical illness or injury, which can readily prove a serious deterrent to speedy recovery or satisfactory resettlement in industry. Anxiety about personal or domestic affairs, fear of losing one's job or becoming a permanent invalid, or opportunity to exaggerate symptoms as a means of escape from social obligations—all such factors may hinder successful rehabilitation unless wisely and sympathetically handled. It is here that the almoner or welfare worker, with her special training in social science and her long experience in dealing with individuals, can render such important service. If rehabilitation is to constitute an integral part of the future hospital services of the country, it is obvious that the almoner's department must be strengthened in every hospital (or speedily established, if not already in existence) and that these social workers must be set free from much of the routine financial work which at present absorbs so much of their time. It is only by sympathetic understanding of a patient's circumstances that his confidence can be won, his co-operation in his own recovery secured, and he can be guided back to a useful place in society.

ASSESSMENT OF FUNCTIONAL CAPACITY

There is a further duty which is laid upon our hospital services, in helping to implement the Disabled Persons (Employment) Act, namely the provision of scientific guidance as to the exact functional capacity of any patient who is disabled by reason of his illness or injury and will never be able to return to his former occupation. The actual responsi-

the more severely disabled must be transferred for the final stages of their physical reconditioning, as described later in this paper.

(2) *Range of medical and surgical disabilities suitable for active rehabilitation.*—There is an unfortunate impression, widely prevalent, that active rehabilitation is only applicable to orthopaedic disabilities and traumatic surgery. This misapprehension largely derives from the historical fact that modern methods of physical rehabilitation sprang into popularity with the successful and brilliant work of Robert Jones and his orthopaedic colleagues during the war of 1914-18, and that the B.M.A. Committee on Fractures and the Delevingne Commission confined their recommendations to the setting up of rehabilitation departments in connexion with fracture clinics and the treatment of persons injured by accidents. The experience of this present war has proved that rehabilitation should not, and must not, be confined within such narrow limits, and that the same principles apply equally to all forms of medical and surgical disability or loss of physical and psychological function, resulting from prolonged immobilization or severe illness. Encouraging results have already been obtained by the scientific application of these principles to a variety of chest complaints, including chronic bronchitis and emphysema, asthma, pneumonia, empyema, and the after-treatment of lobectomy, pneumonectomy and thoracoplasty; to the recovery of abdominal muscular tone and the prevention of liability to hernia or prolapse after laparotomy or childbirth; to the rapid and complete recovery of the mobility of the fingers and hands after septic infections and burns; to the treatment of certain forms of arthritis which have reached a chronic stage, with a normal blood sedimentation rate; to the psychological readjustment of patients suffering from various manifestations of psychoneurosis; and to the partial or complete restoration of function after injury or disease of the central nervous system. In this last connexion, the brilliant results which have been obtained at Stoke Mandeville, in the treatment of spinal paraplegics under Dr. Guttman's leadership, have proved convincingly that even so apparently hopeless a case as the patient with destruction of the spinal cord, and with complete loss of function of bladder and rectum and lower limbs, can yet be got on to his feet and enabled to take up useful forms of gainful occupation, as the result of a scientifically devised programme of thorough rehabilitation and vocational training.

(3) *Appointment of trained staff.*—The provision of an adequate hospital rehabilitation service in a hospital is not a matter which can be safely left to the haphazard device of any physiotherapist who happens to have been practising massage and electrotherapy there over a course of years. It is essentially a scientific form of treatment which is constantly changing and improving its technique, and can only be properly entrusted to a trained staff, thoroughly conversant with modern methods. At the head of such a staff there should obviously be, wherever possible, a specialist in physical medicine, to whom the actual superintendence of all forms of rehabilitation treatment should be delegated by the physician or surgeon in charge of the case, and who should have a free hand in ordering the particular forms of physiotherapy, physical exercises and occupational handicrafts best suited to each patient. In hospitals which have no physical medicine expert on the staff this duty is often entrusted to an orthopaedist, a surgeon in charge of the fracture clinic, or a resident medical or surgical officer, but it is an important principle, which war experience has abundantly confirmed, that this function should always be discharged by a single medical officer, who should be responsible for the training and general supervision of the various ancillary workers, and who should do everything possible to weld them into a united team.

Regular conferences on the problems presented by various types of disability, and the particular part which physiotherapy, group exercises, remedial games and occupational therapy severally play at each stage of recovery, are an important means of educating and uniting such a team, and should constitute one of the duties of such a rehabilitation medical officer.

(4) *A balanced and progressive programme.*—If rehabilitation is to be carried out scientifically and efficiently, it is essential that a carefully thought-out programme should be laid down for each type of medical and surgical disability and for each successive grade in the process of recovery. The basic principles underlying such a programme are fundamentally the same, whatever be the nature of the disability, combining as they do the use of physiotherapy and active exercises, remedial games and appropriate occupational handicrafts, alternating with prescribed periods of rest, relaxation and mental entertainment. The actual programme for each patient must, however, always be an individual matter, and must be related, not only to his particular illness or injury, but also to the type of work which he normally follows and to which he hopes to return. In the case of heavy manual workers, with reasonable expectation of being sufficiently restored to be able to resume their former occupation, it is obvious that the programme of rehabilita-

what is done in the hospitals in the form of medical rehabilitation. Successful rehabilitation needs a full partnership of patient, doctor and employer. The House may be surprised to know that more than 11,000 patients in Emergency Medical Service hospitals are now taking daily courses of remedial exercises in the wards. In addition, a further 20,000 attend the hospital gymnasium daily for special exercises and remedial games. Of these 31,000 receiving daily rehabilitation, 15,000 are also taking part in some form of occupational therapy. I think the House will agree that these figures are an impressive indication of the large measure of progress which is being made. Since my department made a special survey, in 1943, with the object of extending these facilities, the number of hospitals providing rehabilitation for their patients has increased from 150 to over 300. The great majority of Service sick and wounded received their medical rehabilitation in E.M.S. hospitals. More than 250 doctors have been given special courses of training, and for hospitals handicapped by lack of accommodation—a very serious difficulty—the Ministry have provided 34 pre-fabricated buildings. Conferences have been held throughout the country for leaders of industry, personnel managers, welfare officers and industrial medical officers, to explain the whole process of rehabilitation, and the part which industry has to play in the resettlement of patients.

Most of the cases to which I am referring concern wounded men, but there are also many surgical and other conditions where the rehabilitation we have in mind, as forming an essential part of the health services of the future, must be included. We shall not relax in this matter. The Ministry of Health will retain their rehabilitation department, and we shall endeavour to encourage rehabilitation as an integral part of the health services of the country."

We have yet to see how far this forecast will actually be reflected in the terms of the new Health Bill, but there is no reason to suppose that rehabilitation will be omitted from the provisions of that Bill. The necessity of providing facilities for hospital rehabilitation by the Ministry of Health is also specifically referred to in the White Paper which forms the basis of the Industrial Injuries Bill now before Parliament. It will obviously take some years before the necessary buildings and staff will be available for the carrying out of such a comprehensive scheme, but it is becoming increasingly clear that it will involve the provision of four types of medical rehabilitation centres:

(a) An efficient physiotherapy department at every hospital, with adequate accommodation, special equipment and trained staff, sufficient to give proper rehabilitation to all its in-patients. This should be a minimum requirement everywhere, and no hospital should be allowed to treat patients insured under the new health service which could not provide these facilities.

(b) A large out-patient rehabilitation centre (or centres) in every town or district, capable of receiving and treating patients attending the casualty or out-patient departments of the local hospitals who need daily rehabilitation to hasten recovery; former in-patients of the local hospitals who have been discharged from the wards owing to pressure of bed-space before being fit to return to full work; and non-hospital patients, referred by private and panel doctors and by industrial medical officers. Such out-patient centres would normally be situated at one or more of the local hospitals, where adequate accommodation was available; or could be set up by the joint action of more than one hospital; or could take the form of combined health and rehabilitation centres, under the health authority, drawing their expert staff from the consultants of adjacent hospitals.

(c) Residential rehabilitation centres, outside the town, to which all patients requiring long-stay rehabilitation could be transferred for the purpose from the hospitals in the neighbourhood.

(d) Special rehabilitation centres, scattered throughout the country, for the rehabilitation of particular disabilities. These would naturally include the orthopaedic hospitals for children; sanatoria and colonies for patients with pulmonary tuberculosis; centres for psychoneurotics; medical training centres for epileptics; centres with special "hardening" courses for sick or injured workmen from the heavier industries, such as mining and dock labouring; and other centres which will be required in connexion with experimental research in rehabilitation methods for special types of disability such as chronic cardiac cases, spastic paraplegics, chronic skin complaints, arthritis, &c.

It is obvious that the carrying out of such a programme will require a great expansion of trained staff. Many more specialists in physical medicine will be urgently needed, to give direction to medical rehabilitation at these various centres, and it is much to be hoped that many new recruits will be forthcoming from the ranks of medical officers who have taken an active part in physical medicine and rehabilitation whilst serving with the forces. An increased supply of physiotherapists and occupational therapists, almoners and social workers will be needed, including—it is hoped—male occupational therapists trained to supervise the heavier handicrafts and the operation of curative workshops. Physical training instructors and instructresses will both be required, and as a partial solution of that particular problem the Ministries of Health and Labour are now providing an intensive six-months' course in medical rehabilitation for selected P.T. instructors released from the forces, of whom 150 should be available in the course of the next twelve

bility of finding suitable work for such a man—if, indeed, such be possible—or of recommending a suitable course of training for some new vocation, rests upon the Disablement Rehabilitation Officer now attached to all the larger employment exchanges. But the D.R.O., as he is commonly called, has no knowledge of medicine or surgery, nor any previous experience of hospital practice, and must work completely in the dark unless carefully instructed and guided by those who have direct knowledge of the patient's physical condition and the extent and character of his disability. What the resettlement officers require to have at their disposal is a clear report stating, in simple physiological language, just what the disabled person can and cannot do, and what environmental conditions would be prejudicial to his health or likely to cause breakdown at work. Such a report can be supplied in the form of a medical certificate, such as the special D.P.I Form which has been issued experimentally by the Ministry of Labour, and which has been drawn up in such a way that every type of disability can be described in terms of functional capacity. But the ideal method of providing medical guidance in the resettlement of the disabled is not by certificate, but by regular conference between representatives of the hospital and of the employment exchange. I have recently seen what I regard as a model system at a large Local Authority hospital near London. At this hospital all cases requiring rehabilitation are referred by the physicians and surgeons to the specialist in physical medicine, who directs their programme of activities, and who has been provided with his own almoner for dealing with the personal, domestic and economic problems of each patient. A conference is held weekly by this medical director of rehabilitation, the almoner and the local D.R.O., when each patient likely to require vocational training for some new occupation is brought under review, and explicit recommendations as to suitable work are thus based upon the medical officer's intimate knowledge of the man's disability and functional capacity, the almoner's knowledge of his domestic and financial position, and the D.R.O.'s knowledge of available jobs, or possible courses of vocational training.

Periodic follow-up and review.—Once the disabled person ceases hospital treatment he becomes the responsibility of the Ministry of Labour, whose officers, aided and guided by the medical reports and recommendations above referred to, have to try to find suitable employment, appropriate to his reduced capacity or loss of particular function. In some cases this is merely a matter of looking for a vacant post in which the disability will not prove a handicap, e.g. a sitting job for a man or woman who can no longer stand at work all day, or work in an air-conditioned factory for the patient with chronic chest trouble. In other cases, however, it will involve a preliminary course at a training centre, in order to be fitted for some quite new occupation, or the provision of employment at one of the sheltered workshops which are to be established under the Act.

But whatever the route by which the disabled person reaches suitable occupation, his successful performance of his new task will depend upon his being able to stand up to the physical or nervous strain which it entails; and if wrong placement is to be quickly spotted, and cases of undue strain speedily relieved, careful supervision and periodic review are essential. In many cases this supervision will be maintained by an industrial medical officer or personnel manager, if the patient happens to be working in a large industrial organization provided with such officers. The employment exchanges will also be interested in following up the results of their placements in industry. But rehabilitation is primarily a medical problem, not an industrial one, and it is the hospital which actually treated the patient and saw him through to the point at which he was to be fitted out for a new job, which always ought to take the initiative in following up its cases, and arranging for a return to hospital and careful review of every case in which there is any doubt of ability to make the grade.

THE FUTURE OF HOSPITAL REHABILITATION

The foregoing consideration of the clinical implications of the Disabled Persons (Employment) Act should make it clear that for the successful implementation of the Act, the setting up of a comprehensive system of hospital rehabilitation will be needed throughout the country. But this is not the only reason for anticipating a great expansion of rehabilitation facilities in the future. The White Paper on National Health Service specifically mentioned rehabilitation as one of the medical benefits which should be covered by the health insurance scheme and which insured persons would therefore have a right to claim, and in his last report to the House of Commons on June 12, 1945, the former Minister of Health, Mr. Willink, made the following important reference to the subject:

"I should like to say something about rehabilitation, because I do not think it is generally realized how much this has been developed during the war in hospitals within the Emergency Medical Service. The House has been concerned, through legislation introduced by the Minister of Labour, with the great question of industrial legislation and resettlement, but, of course, everything that is done in this field must depend upon

Concerning the fuller development of a policy to link hospitals with industry the Act has little to say; it is suggested (by the writer) that this should become a responsibility of District Advisory Committees.¹ The D.R.O. is the present link, but so far—for reasons out-with his control very often—the system has not been a success. This fact is one which the National Advisory Council¹ must face up to, and if necessary provide an alternative remedy. Hospital authorities may therefore have to consider the possibility of appointing their own industrial liaison officers—persons with practical experience of factory work, but not necessarily with medical or nursing qualifications—who would not only provide a link with the patient's employer but advise the surgeon concerning job-allocation in relation to the physical and mental requirements of different occupations. How many physicians or surgeons, for example, have ever seen a man operating a capstan lathe or a hydraulic hammer, or know the work of a moulder in an iron foundry?

THE CONTRIBUTION OF INDUSTRIAL MANAGEMENT

No matter how efficient the hospital, how good the treatment, and how much contact the social service or almoner's department has with the factory there can be no effective return to work, and therefore no full rehabilitation and implementation of the Act, without the co-operation of the employer. His contribution must include the following:

(a) The promise of continued employment can remove the fear of insecurity, a potent means of retarding recovery. It is a fact that many disabled workers already in employment are unwilling to put their names on the Register of Disabled Persons because of the fear of losing their job. Some statement from employers' organizations may therefore be necessary at an early date.

(b) A promise of alternative work can be made if the employee is unfit for his pre-accident job. To be effective this must be true alternative work under medical supervision and not light work specially created as a charity.

(c) The possibility of re-training for alternative work should be considered. This can only be done in the larger firms; Government Training Centres and certain extra-industrial centres can theoretically cover the remainder of industry.

(d) Assistance on matters arising under the Workmen's Compensation Acts is important. The present Acts, although financially more attractive within recent years, can still do much to retard recovery particularly in long-continuing cases by creating distrust of the employer on the part of the worker. Some insurance companies have contributed in no small way to this. But even with the new Industrial Injuries Act there will be much help required from management. The employer's fear of the consequences of yet another Government department coming into the day-to-day routine of industry is very real; not only can this still further widen the gap between employees and employers, but by its very cumbersomeness cause irksome delays and difficulties. So there is real need to provide some human link between the Ministry of National Insurance, the Ministry of Labour, and industry.

(e) It is important that employers should appreciate the fact that a man cannot be unfit one day and on the next, in a different environment, be really fit for full work. The goodwill of managers and foremen (the real executives of industry) must therefore be obtained for the worker during what is often an awkward phase in recovery—that period of time between being signed off by the insurance practitioner or the hospital and returning to his original occupation.

(f) The provision of rehabilitation workshops in the larger organizations, e.g. every factory or group employing 5,000 workers or more (to include medical as well as surgical cases), or on a regional basis by the institution of communal rehabilitation factories linked with hospitals,² must be fully considered.

Personnel management and rehabilitation.—It should be a primary responsibility of personnel management, under the present system, to play a part in the supervision of the return to work of the sick or injured worker. This applies to all types of industry, and to all sizes of organization. In the larger firms personnel management and industrial medical service must work in the closest collaboration. One cannot function efficiently without the other. In the smaller industrial unit, e.g. the factory with less than 300-400 employees, there is usually no special official appointed as personnel or welfare officer and this function therefore becomes the direct responsibility of the works manager. Because the majority of firms in this country come within the "small" category, and

¹ See Disabled Persons (Employment) Act, p. 10.

² A scheme for communal rehabilitation workshops has been planned for Birmingham and will be published at a later date by Mr. W. Gissane and the writer.

months. But the greatest need of all will be the inclusion of regular instruction in rehabilitation as part of the ordinary medical curriculum, and the integration of this important development in social medicine in the education of all future members of the medical profession.

Dr. Donald Stewart, Birmingham: Industrial rehabilitation.—Section 3 of the Disabled Persons (Employment) Act, 1944, promises facilities for "industrial rehabilitation courses". It lays down that these will be for disabled persons over 16 years of age who are unfit because of injury, disease, or deformity and who need such facilities to render them fit for their previous work. At these courses, according to the Act, will be provided (a) physical training and exercise, (b) occupations conducive to restoration of fitness, and (c) other incidental facilities—all to be under adequate medical supervision. Where exactly the courses are to be held is not yet known, but if special centres are set up for the purpose the expense to the country must be fully justified. Physical training and exercise can be adequately provided at hospitals and at rehabilitation centres. Occupations "conducive to restoration of fitness" can be provided on a small and relatively unimportant scale in rehabilitation centres (although this needs further expert advice and planning) and in sheltered environment such as that already provided for cases of tuberculosis; but, most important of all, they can be provided, and provided well, in normal industry and in special rehabilitation shops and factories.

The implementation of the recommendation in the Act which states that all this is to be under medical supervision is of special significance and needs emphasis. Rehabilitation is an essential part of treatment and to be successful it must, in all its stages, be under medical control. That phase which is now termed industrial rehabilitation, therefore, must also come under medical care until the patient is fit for his pre-accident or pre-sickness employment, or has been satisfactorily trained for other work. This is a challenge to medicine from the workpeople of this country which must be fully understood and accepted by those responsible for planning the new national health service. Present facilities in industry for rehabilitation under medical supervision are to be found only in those firms that have developed their own medical service, and from present practice in industrial medicine much can be learnt concerning the clinical implementation of the new Act. Conversely, the future development of industrial rehabilitation, and this includes its interpretation under the Act, must be accompanied by medical supervision at the place of work, that is, by a comprehensive industrial health service. Without this the new legislation cannot be fully implemented from the clinical point of view and will largely fail—in spite of the elaborate machinery that has been set up.

HOSPITALS AND INDUSTRY

Hospital services deal in the main with anatomical and functional recovery. Many of them are now venturing into the social field by changing the outlook and work of the almoner. But the new aim of rehabilitation must be to base it on economic grounds, where the man obtains at the earliest possible opportunity—it may be during treatment—both work and reward; national benefits are only palliative and, under the present system of workmen's compensation or even the new Industrial Injuries Act soon to become law, may actually retard recovery.

Three points relevant to hospitals have a bearing on the industrial side of the problem: (a) With good treatment the need for special rehabilitation measures decreases. Industry is therefore fundamentally interested in the future hospital policy of this country on purely economic grounds. (b) There is a grave risk that "rehabilitation" may be plugged too hard (using the word in the narrower sense) at the expense of earning capacity. Ancillary aids to cure such as occupational therapy may possibly be overdone because they are new to the public (and this includes politicians) and somewhat dramatic. Hospitals may have purchased expensive equipment (e.g. weaving looms) and appointed considerable staff (e.g. physiotherapists and occupational therapists) and it is only natural to provide sufficient patients to fill the department and attempt to justify expenditure. There may also be insufficient strictness of control of the various stages of recovery by physicians and surgeons themselves, who can place too much therapeutic reliance on basketry, weaving, or the manufacture of dog-leads. (c) The policy of setting up social service departments in hospitals is gradually providing an important link with industry. The function of the almoner is changing, and her contact with management on behalf of the sick and injured worker is a real advance in hospital service. On the other hand, industry itself frequently needs contact with hospitals: it must have knowledge of progress of key men for instance, or it may wish to offer special facilities to an injured man to aid his recovery.

determine what types of individual, both healthy and disabled, should be allocated to each job. Factors in job-allocation are age, sex, general physical and mental make-up, arm and leg efficiency, hearing, vision, and general stability, i.e. a simple adaptation of the Pulhems system used in the Services.

(g) He should consider the advisability of having a social service worker on his own staff. This has already been accepted in principle by certain large firms and is a development of some importance in industrial medicine.

(h) The whole-time industrial medical officer should investigate the possibility of setting up a special workshop in his own organization for the rehabilitation of selected sick and injured workers. Selection should be made in full collaboration with hospital physicians and surgeons, who should act in a consultative capacity in this respect and so themselves learn something of industrial conditions. The potential medical contribution to industrial rehabilitation is thus great, particularly in our larger cities. This type of workshop provides one good answer to the problem of rehabilitation and it should essentially develop as a part of industrial medical service. The Austin experiment is an example of this and a brief account of the scheme is given below.

THE AUSTIN EXPERIMENT

A special rehabilitation shop has been set up at a large engineering works in Birmingham (the Austin Motor Company) for injured employees who normally would not be at work, but would be undergoing treatment. The scheme came into being in April 1943, and was primarily organized by the writer as consulting medical officer to the firm, in collaboration with Mr. W. Gissane, surgeon-in-chief, Birmingham Accident Hospital. (This scheme is similar in some ways to those developed by certain Royal Ordnance Factories during the late war, and to the scheme evolved by Mr. A. H. McIndoe and Mr. George Reid for R.A.F. casualties at East Grinstead.)

The demand.—During the war this firm employed 30,000 workers and had over 1,000 "reportable" accidents annually, i.e. that lose three days or more. By spot surveys it was assumed that at any one time, i.e. on any one working day in the year, some 30 to 40 injured workers could be given "alternative" work in the Shop during the period of treatment, and this assumption has proved to be reasonably correct. The average number in the Shop during the past two and a half years has been 30 to 35. It is interesting that even although the number of persons employed and the number of accidents have decreased since the war ended, the Shop is still kept busy and full.

The link with treatment.—Under medical supervision this work has a definite therapeutic value, and comes within that part of rehabilitation already termed occupational therapy. An essential part of the experiment has been that the surgeons of the Birmingham Accident Hospital act in an advisory capacity to the firm's medical officer on the clinical side of the work, including selection of cases, selection of occupation, follow-up, and progression in occupation until the "patient" is fit for his pre-accident work, or is fully retrained for other work in the factory. Thus a partnership between hospital and industry has been created. The following cases illustrate the value of the Shop.

(1) *Example of occupational therapy and progression from job to job.*—A man has a simple fracture of the left radius and ulna. It is not necessary for him to be treated as an in-patient at hospital so he attends regularly at the out-patient department. Even by the best treatment and rehabilitation methods it will be fourteen weeks before he is normally fit for work. Such a case can be admitted to the Shop in seven days, given at first a one-handed job, then a job where he needs slight movement in the injured part, and gradually progressed through the Shop until he has full function.

(2) *Alternative work for patients awaiting treatment, who would normally be unemployed.*—A girl sustains an extensive laceration of the muscles of the right leg and foot. She has treatment in hospital as an in-patient for ten weeks. This period cannot possibly be cut down. It is then found that to give her a good foot again she must have a plastic repair. The surgeon decides that this cannot be done for at least three months until her tissues regain their vitality. Normally this girl would be out of work during that period. She is admitted to the Shop and three months' work is saved.

(3) *Retraining of permanent cripples.*—A pre-war tailor, employed as a machine operator, loses all the fingers of his right hand in his machine. He is successfully treated by the surgeon, but to all intents and purposes is a one-handed man thereafter. He will be unable to become a tailor again, and is not unnaturally afraid to work on moving machinery. His confidence has gone, and he develops an anxiety state. He is eventually persuaded to enter the Shop and is given bench work such as filing, frazing and scraping, and so he is gradually re-educated to a confidence in the use of machinery which will enable him to be fully retrained as an effective machine worker.

The Shop.—The Rehabilitation Shop is situated near a main gate of the works and near the canteen. From the industrial hygiene point of view working conditions are good, e.g. lighting, heating, ventilation, clothing accommodation, colour schemes, sanitary

because over 50% of factory workers (comprising 75% of productive industry) are employed in units of 250 or less, the education of works managers and foremen in the meaning of rehabilitation, and the part they must play in it, becomes increasingly important.

Light work or alternative work.—A number of firms have appreciated the need for "light" or "alternative" work and have provided facilities within their own limitations; but there is no doubt that the finding of such work is a matter of considerable difficulty taking industry as a whole, and in the small organization is frequently impossible. In certain large firms, however, a number of occupations are specially allocated for convalescent sick and injured patients as part of general welfare schemes. The main criticism of this procedure is that cases are often not under adequate medical control, and that this "allocation" becomes a method of dumping and "losing" unwanted workers often to reduce the so-called "compensation costs".

Objections to alternative or light work can be summed up as follows: (a) It is frequently hit-or-miss therapy; (b) it is difficult to find in the great majority of industries; (c) it is difficult to keep under medical control, and may actually be harmful to the patient by retarding or even permanently interfering with full functional activity; (d) it is frequently not liked by managers, foremen, and by workers themselves, as the productive effort of the industrial unit—the gang or team—may be interfered with by the presence of a semi-fit man; (e) managers and foremen may resent the increase in overhead expenses; (f) the patient is apt to be "lost" in the works and frequently never returns to his pre-accident work; alternative work, therefore, can conceivably become nothing more or less than a scrap-heap for the partially disabled man; (g) it is sometimes created at the special request of the insurance company concerned, where lump sum settlements are involved, as a basis of argument in the County Court in favour of lower settlement.

THE CONTRIBUTION OF INDUSTRIAL MEDICINE

In firms where an industrial medical officer is employed supervision of return to work of the injured or sick worker is one of his primary duties. So important is this work that it is a main reason for the extension of medical services to cover the whole of industry. He can contribute to the clinical implementation of the Act in a number of ways:

(a) He should obtain accurate information not only of the incidence of sickness and accidents but of the progress of all sick and injured workers. The value of a good record-keeping system is therefore emphasized.

(b) He should devise a method of reviewing progress, as required, with hospital staffs and with insurance practitioners. To this review his special knowledge of the work to which the sick or injured worker will return is a valuable contribution; his advice may only be useful in a proportion of cases to begin with, but the number will grow. He should look on the local hospital as his base; medical departments in industry should become outposts of hospitals and not work in isolation.

(c) All accident cases absent for three days or more should be seen by him before recommencing work.

(d) All sickness cases absent three weeks or more should be seen by him before recommencing work. To carry this out effectively he should establish close liaison with local general practitioners. Later this can be done through health centres.

(e) He should develop an adequate follow-up service in connexion with (c) and (d), and in this part of his work the help of a good nurse is of much importance.

(f) He should compile a list of the different occupations in his firm, analysing jobs from the health point of view and in relation to capacity for work, with a view to providing alternative work for specially selected cases conditional on their being under his medical supervision. It must be clearly stated that the doctor's contribution to this is one of job-allocation and is dependent on a job-analysis schedule being provided by industry. This development in medicine is therefore a two-way process, and depends for its success on collaboration between management and the medical officer.

For instance in the iron foundry to-day are to be found the following occupations: annealing, casting, core-making, clerical work, crane-driving, cupola work, dressing (fettling, grinding, trimming, knock-out work), labouring (heavy, medium and light), maintenance (skilled engineering, millwrights), moulding (hand, machine), shot-blasting, truck-driving, viewing (inspecting), and welding. Job analysis of each of these occupations should be carried out by the management, and the results given to the medical officer. It then becomes his responsibility to

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But no mention has been made as to what the Act would cost industry if rehabilitation in its fullest sense were not achieved. It would mean that say $1\frac{1}{2}$ million people would have to be found selected and unproductive jobs at a cost to their employers of some three hundred million pounds a year for "liftmen and lavatory attendants".

Dr. Balme told us that the Ministry of Labour had introduced a form, the D.P.1, which when filled in by the doctor, would give the D.R.O. a functional analysis of the patient's ability to perform the manoeuvres of work. Dr. Stewart told us that the job analysis had not been accomplished but that he thought that it would be a relatively simple item. On this latter point I venture to disagree.

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Very interesting slides of the rehabilitation workshops at the Austin Works emphasized the value of this phase in treatment. In my own opinion the rehabilitation workshop has a greater educational value than a curative value. In those shops both doctor and labour managers learn much of the physiology of job analysis and of the capacity for work of their patients. Whereas certain special cases will always require a rehabilitation workshop for their quickest and best rehabilitation, the majority of cases will do better on alternative work within the industry.

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conveniences, washing facilities, seating facilities, and rest pauses. The "hours of work" are 8 a.m. to 5.30 p.m., and 8 a.m. to 12 noon on Saturdays. The lay-out of the Shop was designed by the Production Director of the firm, and the machinery installed is of a modern type, e.g. no overhead belting. The importance of adapting the plant and machinery to the needs of the injured limb was specially considered by the firm's medical advisers, the Accident Hospital staff, and the management.

Occupations suitable for crippled workers, e.g. with one arm, hand or leg out of action were selected as follows:

Hand and automatic milling.
Drilling of all types.
Capstan work.
General centre lathe turning.
Spot welding, worked by either hand or foot.
Lining. (This can be done with either hand.)
Fly presses.
Electric arc welding. (This for a one-armed man.)
Automatic screwing.
Surface grinding.
Soft soldering.
High pressure gas welding.
Bench work including: Filing; hand dyeing; counter sinking; fraizing; scraping; assembling; hand pressing.

Examples of products manufactured in the Shop are:

Oil strainers for all engines produced by the firm.
Starter nuts for all engines produced by the firm.
Spring pins.
Brake levers.
Bolts of different types.
Work trays.
Barrel nipples for oil pipes.

Management of the Shop.—A trained and experienced engineer was appointed to be the Shop manager. Before commencing work he was given an opportunity to appreciate the surgical, social and economic background of the accident problem as it exists in this country, and with this in view visited different rehabilitation centres and hospitals. It was considered that this appointment was of vital importance in the experiment, as any success that might be obtained would in a large measure be due to his personal efforts. After two and a half years' work this has proved to be the case and those of us connected in any way with the experiment must pay tribute to the way in which he has carried out his work.

Payment and incentives.—A payment method known as the "2-4-6 system" has been used. If a man receives say £2 a week on compensation and his average pre-accident earnings are £6 a week, it was proposed that his payment in the Shop should be not less than £4 per week. This means that he has a double incentive: (a) to earn more than he would on compensation and so be attracted to work in the Shop; and (b) to strive towards his pre-accident rate. The man is only in the Shop during such time as he is certified for such work by the surgeon. He returns eventually to his pre-accident work, or to other full work for which he would be suitably trained, in other parts of the factory.

Examples of payments are as follows (as at July 1943):

	Pre-accident rate			Shop rate*		
	£	s.	d.	£	s.	d.
Case 1 (female aged 29)	4	17	9	3	16	6
Case 2 (female aged 17)	3	0	9	2	7	9
Case 3 (male aged 41)	6	14	6	5	8	6
Case 4 (male aged 16)	2	3	10	1	15	6
Case 5 (male aged 30)	7	15	2	5	14	6
Case 6 (male aged 56)	5	4	5	3	9	6

*The Shop rate is made up as follows: flat rate, plus cost-of-living bonus, plus any compensation for which he may be eligible under the Acts.

Results.—During the two and a half years of its existence the Shop has employed over 500 injured workers. The majority of these were patients of the Birmingham Accident Hospital. Approximately 80% of cases returned to their original work; 10% to a different job because of change of products of manufacture due to the ending of the war; 5% were retrained for other work; and 5% transferred to other work because of their disability, no special training being necessary.

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the results are not statistically significant because of the thousands of possible jobs and degrees of cardiac disability. What is most needed for resettling disabled workers is a comprehensive job analysis for all occupations in the country. Apparently the Ministry of Labour is not tackling the problem itself, but is relying on the spasmodic efforts of individual firms. No real results are expected for five to ten years.

A possible alternative is for the doctor who knows the case of a disabled man to prohibit specifically certain physical actions, such as lifting weights of more than 20 lb. The new Ministry form "D.P.I." now in experimental use has this as its basis, it is very helpful, is easy to use, but is not yet approved by the B.M.A. and may not therefore come into general use. Much more must be learned by doctors and labour officials of the capabilities of the medically disabled and the physical requirements of industrial occupations.

Sir Reginald Watson-Jones was glad to have heard constructive criticism of the steps which had been taken to implement the Disabled Persons Employment Act because, as Chairman of the Medical Committee of the National Advisory Council, it was his duty to advise the Ministry of Labour and National Service and no one who applied his mind to these problems could believe that they were easy of solution. At an earlier stage the Ministry had been advised that disability analysis on the one hand and job analysis on the other were all that was necessary. But so simple an equation was impracticable. In most cases the resettlement of disabled persons called for very skilled medical experience coupled with a knowledge of industry. Disablement Rehabilitation Officers could be trained to appreciate the industrial problems, and special courses were being arranged by which to improve the service of a group of men and women who had done all that was possible during a period of acute man-power stringency. Nevertheless it was obvious that medical direction was also essential and the Ministry of Labour had now been advised that Disablement Rehabilitation Officers should be directed by local medical boards and their activities co-ordinated by regional medical consultants, so that disabled persons would be guided to the type of employment most suited to their disabilities. Every doctor who shared in treatment could make a valuable contribution. There was danger that the Act might fail by reason of the failure of disabled persons to register. Patients who had been well treated might reasonably hesitate to accept the label of "disabled"; and yet if they did not register the quota which gave them the right of employment would be misleading. Dr. Balme had indicated that there were probably from one to one and a half million disabled persons in this country; but at the present rate of registration many years would elapse before this number was on the register and the quota reliable. Doctors should so influence their patients that a complete record was available of every individual who might have difficulty in seeking or keeping employment. If this were *not* done one of the greatest medical and social reforms of this generation would be imperilled.

Section of Experimental Medicine and Therapeutics

President—E. N. ALLOTT, F.R.C.P.

[December 11, 1945]

DISCUSSION ON D.D.T.

Professor G. R. Cameron opened the discussion. His paper was published by the British Council (*British Medical Bulletin*, 1945, 3, 233) and summarizes a much longer paper which appeared in the *British Medical Journal* of June 23, 1945, p. 865.

Dr. Herbert D. Chalke, late Colonel R.A.M.C.: My contribution is a brief account of the use of D.D.T. in the field during the Italian Campaign, particularly during the Naples typhus epidemic, and as an anti-malaria measure. All this has become ancient history, but you may be interested to hear something of the experiences and difficulties during the days when we were experimenting with an insecticide which was rather an unknown quantity.

The Naples typhus epidemic.—Naples when we occupied it in October 1943 was a very sad city, badly bombed, overcrowded, with a depressed and undernourished populace living in considerable numbers permanently in shelters. Below the streets of Naples and on the outskirts of the city are innumerable caves and tunnels, many dating back to ancient times. These were the permanent homes of thousands of people. Naples seemed to be the perfect stage setting for a large-scale epidemic of a disease such as typhoid or typhus. Means of heating and lighting were lacking, the water mains and sewers were ruptured, and a large proportion of the people were lousy. For example, the largest civil hospital housed almost a thousand patients, all said to be infested. The public services, including the public health and practitioner services were quite disorganized, despair and apathy ruled the land. Under these circumstances it was hopeless to expect any but the scantiest of infectious disease statistics. The Allied Military Government (A.M.G.) commenced to function at an early date, and their medical officers worked magnificently in trying to restore the medical services to normal. My main fear was of an outbreak of typhoid, but fortunately this did not occur in Naples, although other towns were severely affected. We were on the lookout for the occurrence of typhus cases, and on November 20 information was received that 7 cases had been reported in the city. A conference was called the next day and a committee appointed to investigate—it consisted of Allied and Italian medical officers. Clinical examination of the cases suggested that we were, indeed, dealing with classical typhus. Although at that time no information as to previous cases could be obtained from the Italian doctors, documents were brought to light at a later date that made it clear that sporadic cases had been occurring since March. It was said to have been introduced by Serbian Prisoners of War who were scattered throughout the city as a result of Allied bomb damage. Civilian cases occurred in July—a man visiting a bathing place used by troops, who returned home lousy, was the first case. Afterwards cases occurred in jails, but many prisoners—contacts—were said to have escaped and were not traced. The Allied Committee arranged for the setting up of disinfection and bathing centres, but all the principal disinfestors had been destroyed by bombing or enemy sabotage. Fuel and soap were almost unobtainable. Indeed, soap was extremely scarce throughout the epidemic, and the populace remained unwashed, in particular the 20,000 shelter inhabitants. Application was immediately made to higher Allied Authority for supplies of soap and insecticide powders.

Progress of the epidemic.—

November 17 to 30	36 cases
December 1 to 7	22 cases
December 8 to 14	45 cases
December 15 to 22	36 cases
December 23 to 28	138 cases

It was evident that a severe typhus outbreak was about to occur among the million inhabitants of Naples.

The situation was serious. Naples had a very large Allied troop population, and it was the main port of Italy, which it was vital to keep open during this critical stage of the Italian Campaign and the eve of the Anzio landings. Hygiene sections played an admirable part at this, and subsequent stages of the epidemic, in constructing baths, disinfection centres and improvised steam disinfestors, and in controlling the insecticide dusting of the 30,000 odd Italians employed in British messes, ordnance factories,

workshops, and on the docks. They also worked in collaboration with A.M.C. in dusting refugees and typhus contacts in the Army areas. Drs. Soper and Davis of the Rockefeller Foundation arrived in Naples early in December. Case searching, contact delousing and block dusting commenced at once under their direction.

Teams of trained civilians dusted shelter-dwellers. Brig. General Fox and the U.S. Typhus Commission commenced work early in January; a mass delousing scheme was rapidly organized and energetically pursued. Twelve public centres were soon functioning, inoculation was commenced, and propaganda increased. This work was handed over to the Allied Commission on February 19.

Drs. Soper and Davis, who did admirable work, used American Service "M.Y.L." insecticide by means of hand dust guns of the "Hudson Admiral" type. During this period only about 10% of the dustings were done with D.D.T. (10% in talc). 5,000 dustings (approx.) were carried out during this time, about 3,000 of them were on typhus contacts. The principle of mechanical dusting was quickly taken up by us, using AL 63 powder. Power units were also obtained from local garages and experimented with. The British Hygiene Services were responsible for the 30,000 civilians in their employ, and for the Italian Army (who had a high infestation incidence and a correspondingly high typhus morbidity rate at the early stages of the outbreak) as well as refugees and British Troops. Yugoslav prisoners were hospitalized under our direction in Italy. Many of these arrived with typhus. All were dusted with AL 63 on arrival, many having been previously dealt with in Yugoslavia before departure. This focus of infection produced no secondary cases in Italy.

The dust gun was such an admirable weapon that we commenced local manufacture, at first by Italian tinsmiths, and later in army workshops. Field hygiene sections also experimented with and turned out quantities of hand and power sprayers. All British troops were dusted with AL 63 weekly. A high standard of cleanliness was insisted on, and the usual regulations about visiting civilian establishments and contact with civilians generally were put into operation. Civilian public places were closed. A local typhus committee and an Allied Typhus Control Board were formed and supervised and directed preventive measures. Unfortunately, the shelter population could not be cleared owing to frequent enemy air raids, and the fact that there was no alternative housing accommodation during the day. This was, however, not entirely disadvantageous, for this section of the population was always available for treatment by the dusting teams who visited caves and shelters periodically.

After many difficulties the infectious disease hospital—badly bombed—was put into operation for housing the patients. A section of this was staffed by Lieut.-Colonel Stuart Harris, R.A.M.C., and his team assisted by 12 British Army Nurses, and members of the Friends Ambulance Unit. The work of these people, under conditions of extreme difficulty and a high degree of personal danger, was excellent. The U.S. Typhus Commission was assisted in the case searching, contact delousing and inoculation schemes by a number of R.A.M.C. Officers. British and U.S. Ambulances were used to augment the limited and indifferent Italian transport, but transport arrangements for the Typhus Commission personnel were inadequate throughout. From January 1 all mass and contact civilian dusting was done with D.D.T. under the organization of General Fox, U.S.A.M.C. (Up to a maximum of 70,000 daily, exclusive of the dusting with AL 63 of civilian employees and refugees.) The populace needed no compulsion to avail themselves of the service; they soon learned that almost immediate freedom from irritation resulted, and they gladly welcomed the change.

Subsequent progress of the epidemic.—Up to about January 9 cases rose rapidly to 65 daily, but afterwards there was a dramatic fall from 340 per week to half this number. At this time, Naples was placed out of bounds to all the Allied Forces except those on necessary duty. The curve remained steady for the ensuing three weeks, after which it again fell sharply to 40 early in February, and thereafter the epidemic gradually declined. 1,600 cases occurred in all. Cases outside the city increased at this time and continued for many weeks, owing to the imperfect control of civilian movement in and out of the city. There can be no doubt, taking into account the twelve-day incubation period, and the fact that few cases were notified before the fourth or fifth day, that the initial control of the epidemic was brought about as a result of intensive case searching and the ringing of contacts with barriers of insecticide. At this time D.D.T. was used only to a very limited extent. The usual anti-typhus measures employed must also have played an important part. The epidemic, checked by this initial onslaught, was given its final knock-out blow by the large-scale use of D.D.T.

During the whole epidemic only one British case occurred—a deserter, who was heavily infested when apprehended. No case was reported among the 20,000 to 30,000 civilian employees, and few in the Italian Army after December. AL 63 alone was used for dusting these groups.

The fight against the epidemic has been called the second battle of Naples, and undoubtedly, had it not been won, the Allied cause may well have been seriously endangered. Tribute must be paid to all who took part in the battle—the members of the U.S. Typhus Commission, the Rockefeller Foundation workers, A.M.G. and British and American Medical Services personnel, all of whom worked untiringly in full co-operation and harmony.

The lessons learned.—Naples taught us that an army can live and work in an overcrowded, war-damaged, typhus-ridden city, provided adequate precautions are taken. (Up to the middle of January, a relatively small proportion of British troops was protected by inoculation.) It showed us the benefits of mechanical methods of using insecticides on fully clothed subjects, and enabled the cumbersome steam and hot air disinfestors which took up so much transport, to be dispensed with. It also showed beyond question that D.D.T. was a new weapon of tremendous possibilities.

Technique of dusting.—This knowledge was used with advantage in preventing and treating infestation among the troops during the later stages of the campaign in Italy and in N.W. Europe and in dealing with the thousands of Axis prisoners and Allied ex-prisoners who passed through our hands at the cessation of hostilities. There was, however, need for education, and adherents of the old regime were sometimes hard to convince that dusting alone (at three intervals of a week) was sufficient. This was largely due to the fact that since the ova are not affected by dusting, a few lice were often discovered on members of units who had been treated a week previously. D.D.T. does not kill quickly, but its persistent action is a safeguard against the reinfestation which is always liable to occur after steam or hot air treatment of the clothing, although this method kills eggs and adults alike. Mechanical dusting enables large numbers of subjects to be treated quickly. The powder is applied to the head, forced up the arms, down the front and back of the neck and the pubic and gluteal regions. Except in cases of very heavy infestation it should not be necessary to introduce powder between different layers of clothing or to dust blankets and bedding.

MALARIA CONTROL.

The possibilities of D.D.T. as an anti-malaria measure were soon realized, and early in 1943 experiments were commenced in its use on the ground and in the air. An enormous amount of work was done by medical officers of the Allied Control Commission under the direction of Col. Paul Russell, the Rockefeller Team, and British and American malariologists. In addition, Major Cranford Benson, who was in charge of an Entomological Research Unit and who had carried out valuable pioneer work on impregnated shirts, continued his researches on the use of D.D.T. in the field. The information thus gained enabled a technique to be evolved which was put into operation during the malaria season with considerable success. It is believed, also, that the pioneer work was made use of in other theatres of war. The malaria danger in Italy was very great. Deliberate enemy sabotage had resulted in vast areas, like the Pontine Marshes, becoming once again dangerous breeding grounds, and the menace of a flooded Po Valley loomed ahead. The war had also brought about a cessation of civilian anti-malaria schemes, and the Italian Army from Sardinia provided a new and dangerous reservoir of infection. Fortunately, our fears of a large-scale malaria epidemic were not realized: the British Army morbidity rate was, in fact, lower than during the previous year. That the risk was there was evidenced by the civilian incidence in the Littoria province where at least 30,000 cases occurred during the summer of 1944 out of a population of 240,000. The cases occurred in that part of the province flooded as a result of destruction of pumping stations and canals, where the mosquito population was enormous. In similar areas, occupied by troops owing to operational necessity, where D.D.T. spraying was used, comparatively few cases occurred. As the 8th Army advanced, malaria control teams sprayed all houses, cowsheds, &c., with anti-mosquito spray using power sprayers. This gave a quick knock-out effect on mosquitoes. They were followed by teams who used 3 to 5% D.D.T. solution in kerosene; knapsack sprayers were used. There is hardly a house or animal-shed in Central and Northern Italy which does not give evidence of this on its walls, where the familiar white letters "D.D.T."—followed by the date and number of the malaria control unit carrying out the work—record the work done. The first essential of D.D.T. spraying is to use a coarse spray, and the happy medium between too fine a spray and a wasteful wet spray must be aimed at. It is necessary, therefore, that whatever spraying apparatus is used, the jet be of a suitable size—approx. 1/32 in. The jet of the apparatus should be held from 1½ to 2 feet from the wall surface. Although the lethal action of D.D.T. persists for about three months, spraying as an anti-fly or anti-mosquito measure should be repeated monthly: a quart of a 5% solution will treat 1,000 square feet.

Toxic effects.—No ill-effects were noticed during the treating of more than a million civilians in Naples with 10% D.D.T. in talc, neither were the operators who were always white with dust adversely affected. Masks, gloves and gas capes were used by the Army operators of D.D.T./Kerosene solutions, because exact information as to the toxicity of these solutions was not known. Two workers were affected, but the symptoms were suggestive of heat-stroke. It is considered that reasonable precautions should always be taken, not only because of a possible D.D.T. absorption, but also against a kerosene risk. Mechanically unsound apparatus in which there is much leaking should not be used: it is wasteful and adds to the risks of the operator.

Paints and distempers.—The use of oil-bound water paints and distempers in which 5% D.D.T. is incorporated were experimented with. This method of treatment of cookhouses, messrooms and latrines has great possibilities.

CONCLUSIONS

D.D.T. is undoubtedly the most remarkable insecticide yet produced and provides the worker in preventive medicine with a new weapon of tremendous power. It played a big part in protecting our Armies overseas. The knowledge thus gained should be made use of fully in civilian life. But the question must be asked: is it yet safe for general use? Details have already been made known of its lethal effect on benign insects such as bees and ladybirds and even minnows and trout, snakes and frogs are said to have been killed following spraying from the air. Preparations labelled "D.D.T." are now on sale to the public in many chemists' shops, grocers and ironmongers and general stores. The cartons I have seen give no information as to the strength of D.D.T. or the nature of the vehicle in which it is contained, neither are there any instructions as to how the preparation should be used. The public are liable to use it indiscriminately and wrongly, and it is felt that its sale should be controlled, and that full details of the composition of each product should be clearly marked on the container. The suggestion is made that these matters should be dealt with by legislation as quickly as possible.

Major K. R. Hill described a fatal case of D.D.T. poisoning in a child (*see Brit. med. J.*, 1945 (ii), 845).

Dr. R. A. M. Case referred to experiments carried out at the Royal Naval Physiological Laboratory (*see Brit. med. J.*, 1945 (ii), 842).

Lieut.-Colonel F. F. Hellier (late Adviser in Dermatology, B.L.A.): The B.L.A. was the first force to go overseas with D.D.T.-impregnated shirts. They went to France in June and by September cases of dermatitis undoubtedly associated with shirts, began to appear. Recently in Germany as many as 300 to 400 a month have been seen. The dermatitis affected those areas where the shirt was pressed against the skin and in most cases there was an associated purpura on the areas involved. Numerous tests with D.D.T. both as a powder and in various bases were almost consistently negative and I am sure the irritant agent is not D.D.T. as such. We wondered whether some alteration might occur in D.D.T. during washing, &c., but all our investigations have failed to convict D.D.T. It is, however, a striking fact that this rash has been limited almost entirely to B.L.A., which was the one army using impregnated shirts.

The men went over to France in a remarkably clean state, the incidence for both lousiness and scabies being only 1 per 1,000 per month. This state of affairs continued as long as they remained in Normandy, but on moving into Belgium and Holland where they came into closer contact with the civilians, the incidence of scabies, and pediculosis pubis rose by eight or ten times, whilst that of pediculosis corporis remained steady. This could only be attributed to the D.D.T., though why it did not affect pediculosis pubis is difficult to say. As I have shown elsewhere (*see Brit. med. J.*, 1945 (ii), 255) D.D.T. does not affect scabies.

Dr. C. J. Hackett asked Colonel Chalke what dose of mepacrine was being taken in Italy at the time and place in which he said D.D.T. had been so effective in combating malaria. He knew areas in Burma during the war where considerable D.D.T. usage was associated with low malarial incidence and vice versa. At the same time, however, good suppressive mepacrine discipline was practised in the areas of low malarial incidence—and vice versa.

Dr. C. C. Chesterman asked whether there was any pathological evidence of degeneration of the basal ganglia in human beings poisoned by D.D.T. The symptoms suggested it and it would be interesting if a poison so toxic to insects were specific for the more primitive neurons of the brain.

Dr. Chalke (in reply) said that a daily mepacrine tablet was ordered for all fighting troops and certain base troops, but discipline was variable and generally only fairly good. He felt that D.D.T. control had proved effective. Units staging or camping in uncontrolled malarious areas always suffered severely from malaria.

Section of Neurology

President—J. PURDON MARTIN, M.D., F.R.C.P.

[December 6, 1945]

Neurological Experiences in the Middle East and India

By DOUGLAS McALPINE, M.D., F.R.C.P.

NEUROLOGY in the Services in the Middle East and India was mainly concerned with infections of the central and peripheral nervous systems. There were striking differences in the susceptibility of British and Dominion troops as compared with Indian troops. For example, acute poliomyelitis was relatively common in the former, but distinctly rare in Indian troops, whilst in India, acute toxic polyneuritis was rare amongst British troops, but commoner than poliomyelitis in Indian personnel. Diphtheria was so rare in Indian troops that I personally have not met with a case of polyneuritis due to that cause in an Indian. And lastly, meningococcal meningitis was practically confined to Indian and African troops.

MENINGITIS

Meningococcal meningitis.—In India, two factors were responsible for outbreaks of meningococcal meningitis during the winter months. First, the inevitable overcrowding which resulted from the rapid expansion of the Indian Army, and secondly, malnutrition, particularly in recruits to labour battalions. During the first ten months of 1943 approximately seventeen hundred cases were notified. The mortality rate exceeded 15%. An attempt was made between 1943 and 1945 to reduce both the incidence of the disease and the mortality rate, by propaganda amongst O.C.s of Indian units and their medical officers to ensure that there was a minimal delay in cases reaching hospital, and by raising the standard of medical and nursing care in hospitals. Late in 1944, in addition to these measures, a trial of sulphamezathine was made. Early in that year this drug was introduced into India for use by neurosurgical units. It was found that large doses, namely 3 grammes four-hourly, given intravenously, were necessary in order to maintain a C.S.F. concentration of 10 mg.% (Johnson and Dick, 1945). With these doses meningitis in head wounds was effectively controlled. Similar doses were recommended for use in severe cases of meningococcal meningitis. In addition, the feeding of comatose patients by means of an intragastric Ryle's tube, and the nursing of patients in a propped-up position, as practised by Lieut.-Colonel G. Ransome, I.M.S. (1944), in the treatment of cerebral malaria were advocated. A trial of these methods was made in a number of hospitals throughout India. I am indebted to Brigadier B. Schlesinger, Consulting Physician, for the following figures relating to Central Command.

Year	Total	Deaths	Mortality Rate
1943	863	113	13%
1944	418	42	10%
1945 (1st qtr.)	106	7	6.6%

Two of the deaths in 1945 were due to the fulminating form of the disease; sulphamezathine was not given in either of these cases.

Acute benign lymphocytic meningitis.—From 1941 onwards, a lymphocytic type of meningitis was seen in the Middle East in increasing numbers, and at first the classification of these cases was difficult. Many of them closely resembled sandfly fever, but after some months it became clear that in this condition a true meningitis is rare. It was noted that the majority of cases occurred during the spring and summer months. The onset was characterized by malaise, fever, headache, vomiting and a considerable degree of prostration. Neck stiffness was present in varying degrees; Kernig's sign was usually negative. The deep reflexes were normal, depressed or rarely absent. Drowsiness was a feature in some cases, but signs of encephalitis were absent. The average duration of the fever was five days. Recovery was rapid, and no relapses or organic sequelæ occurred. The cell increase in the C.S.F. varied from 20 to several hundred cells, mainly lymphocytes. The fluid returned to normal within three weeks. Neutralization tests in some of these cases proved that the majority were not due to the virus of acute chorio-meningitis. No proof of case-to-case infection was found, nor were there any features to suggest droplet spread; on the other hand no vector could be traced. In 1941 abortive cases of poliomyelitis were reported by Major J. Caughey, N.Z.A.M.C., thus making the sorting out of these cases of lymphocytic meningitis more difficult.

In the latter part of 1941 cases began to crop up which resembled acute benign lymphocytic meningitis, but differed from them in that one or more relapses of headache and

fever occurred after seven to ten days. When, in addition to this feature, a few of these cases developed either signs of encephalitis or facial palsy, it became clear we were dealing with tick-borne relapsing fever.

NEUROLOGICAL COMPLICATION OF TICK-BORNE RELAPSING FEVER

In the Middle East infection occurred amongst British, Dominion and Indian troops particularly in the Western desert, although cases also occurred in Palestine, Syria and Cyprus (Cooper, 1942; Scott, 1944). The strains of spirochæte included *Sp. recurrentis* and *persica*, both of which are highly neurotropic in animals. In order to estimate the frequency with which the nervous system is involved in man, it would be necessary to examine the C.S.F. at intervals in every case of relapsing fever; this was impossible under wartime conditions, but I had the impression that the nervous system was frequently invaded. I have notes of 84 cases in which neurological signs were present:

(a) *Meningitis*.—This occurred in 80 of the 84 cases (95%). It may be noted as early as the second or as late as the eighth relapse of fever. Severe headache is the characteristic symptom. Signs of meningitis are not always present. As a rule with each recurring bout of fever the meningeal signs become more acute. The C.S.F. shows a pleocytosis which may vary from 20 to over 2,000 cells per c.mm. Lymphocytes predominate or may constitute the total cell count. The protein content is increased, sometimes exceeding 150 mg. in the more chronic cases. The W.R. may become positive and the fluid may give a paretic colloidal gold curve. These two findings are sometimes dissociated, the paretic curve being more common than a positive W.R. As a rule the fluid returns to normal within a few weeks of the cessation of fever; rarely the fluid may be abnormal for six months from the onset.

(b) *Meningo-encephalitis*.—24 of the 84 cases (28%) showed encephalitic signs, which appeared between the third and eighth week. Drowsiness is a marked feature; when roused, the patient shows a lack of facial expression and is mentally dull. Diplopia is relatively common. Unilateral or bilateral pyramidal signs may be present, while cerebellar signs consisting of nystagmus, dysarthria and ataxia or tremor of the limbs are not infrequent.

(c) *Facial palsy*.—18 of the 84 cases (21%) showed a facial palsy of peripheral type. It appears between the third and tenth week of the disease and is usually accompanied by fever. In 4 cases the condition was bilateral and in each of these cases a few days to a week elapsed before the face on the opposite side was affected. In only 4 of the 18 cases were definite signs of encephalitis present. Not infrequently there is relative sparing of the frontalis, but otherwise the condition resembles the ordinary form of Bell's palsy. Pain was not a feature, and in those cases in which it was tested, taste was usually reported as normal. Hearing was not affected. In 14 of the 16 cases in which the C.S.F. was examined, a pleocytosis was present.

(d) *Eye complications*.—Papilloedema occurred in 11 of the 84 cases (13%), usually in the later stages of the disease. It was associated with a rise of C.S.F. pressure. With repeated lumbar puncture the condition slowly subsided, but in 3 cases it persisted for some weeks. Loss of vision may be due to a papillitis, to an iridocyclitis or to a uveitis. These complications are comparatively rare.

The following case illustrates some of the complications already mentioned:

Lieutenant R. M., aged 29, left Tobruk on June 25, 1942. About the middle of July he developed fever and this recurred at weekly intervals. On August 24 he was admitted to hospital with severe headache and vomiting of four days' duration. Temperature 100°. Except for neck stiffness there were no physical signs. The C.S.F. contained 485 cells per c.mm., mainly lymphocytes and 100 mg. protein. Blood films were negative for spirochætes. The headache persisted during the next week. At the beginning of September he felt much better, but the C.S.F. showed a strongly positive W.R., with a paretic type of Lange curve. Blood W.R. was negative. He received arsenical treatment, but a degree of headache persisted. The C.S.F. pressure varied between 130 and 170 mm. during the first two weeks in hospital, but by September 14 had risen to 190 and early papilloedema was noted. On September 17 severe headache with meningeal signs recurred. The C.S.F. findings were unaltered. By the end of September he was free from headache and the fundi were normal. The C.S.F. pressure was 140, lymphocytes 33 per c.mm., protein 65 mg. W.R. doubtful. Lange curve 5543331000. He was discharged to a convalescent depot on October 21. On November 26 he reported to hospital feeling quite fit. The C.S.F. was normal in every respect. In this case the spirochæte was never isolated despite many examinations.

On the whole the prognosis as regards neurological sequelæ is favourable. In a small percentage of cases signs of a chronic meningo-encephalitis persist for some weeks after fever has ceased. Headache, impairment of memory, efficiency and initiative may be noted. The C.S.F. is usually abnormal. Since the more chronic cases were evacuated it was impossible to follow them up.

Treatment.—Arsenical preparations were disappointing, both in the early and late stages. However, we had the impression that cases untreated initially were more prone

to develop neurological signs. In future, the effective control of this disease will be possible by the use of penicillin.

ACUTE POLIOMYELITIS

This disease was of importance in the Middle East and India for two reasons. First, it was commoner than in the U.K., and, secondly, there was a high mortality, ranging from 18% to over 30%. In addition, there were facts of considerable epidemiological interest (Seddon *et al.*, 1945; McAlpine, 1945).

Prodromal symptoms lasting two to ten days were the rule. In many cases the symptoms cleared up after two or three days, only to return a few days later and be followed by signs of invasion of the nervous system. This constitutes the so-called dromedary type of prodromata as described by Draper (1917).

These prodromal symptoms could be roughly divided into three groups:

(1) The influenzal group characterized by headache, shivering, malaise, anorexia, backache and pains in the limbs.

(2) The catarrhal group in which some of the above-mentioned symptoms were associated with sore throat, coryza or a cough.

(3) The gastro-intestinal group in which vomiting and diarrhoea were prominent. It is probable that in many individuals these symptoms were not followed by paralysis, but the detection of these abortive cases in tropical countries, except during an epidemic, is a matter of great difficulty. These cases are important since we now know that the virus is usually present in the stools of such cases, and consequently they may play a part in the further dissemination of the disease. It seems clear that in acute poliomyelitis there is a preliminary phase of systemic infection and that the invasion of the nervous system by the virus may depend on local factors in the throat or intestine which favour its passage to nervous tissue.

With regard to the distribution of the paralysis, in the majority of cases the lower dorsal and lumbosacral cord bore the brunt of the disease. The paralysis was often roughly symmetrical. As a rule the muscle groups acting on the hip and knee joints were more affected than the distal muscles. The lower abdominal and erector spinae muscles often shared in the paralysis. In the Middle East and India approximately 50% of all cases had retention of urine; this was usually temporary, but in a small percentage of cases a suprapubic cystostomy was necessary.

Turning to the mild cases, localized and symmetrical paralyses were occasionally met with. For example, I have seen paralysis limited to the masseters in one case, and to the sternomastoids in another.

Fatal cases fell into two groups: (1) The ascending type, and (2) the cervico-bulbar or bulbar type. The ascending type was common in the Middle East and India. The rapid and relentless upward spread of the disease from the lumbar cord in a previously healthy individual was a picture with which we became all too familiar. The majority of bulbar cases were fatal, although a few survived. Death might take place suddenly as in the following case:

Major J. C. B., aged 32, travelled from Delhi to Calcutta on November 27, 1944. On November 30 he complained of headache, vomiting and dizziness. He was admitted to hospital on December 2. His temperature was 100.4°. He was drowsy and complained of headache, but meningeal or other abnormal signs in the central nervous system were absent. The cerebrospinal fluid showed a normal cell and protein content. Fever continued, and on December 5 he complained for the first time of slight difficulty in swallowing, but his speech and breathing were normal. He now showed slight neck rigidity. His condition remained the same until the following afternoon when he asked for a bed-pan. A few minutes later he became incoherent and died. At post-mortem there were changes typical of polio-encephalitis.

We encountered quite a few cases in which the C.S.F. was normal either during the meningitic or paralytic phase of the disease. I roughly estimated such cases to constitute 5% of the total.

Treatment.—The use of iron lungs in tropical climates necessitates either the nursing of the patient in an air-conditioned room, or, less satisfactorily, the reduction of temperature inside the lung by means of ice placed on a tray. A team of medical officers, sisters and nursing orderlies who have had previous training in the use of this instrument is essential. An iron lung is useless in cases of bulbar palsy. Survival may depend on keeping the airways clear, preferably by a rubber tube attached to a suction apparatus; this is not possible with a patient in an iron lung.

Persistent pain in the paralysed limb was frequently met with. Failure to relieve the pain by heat and analgesics, and to maintain a full range of passive movements, resulted in stiff joints.

In India we confirmed the value of a swimming pool during the convalescent stages. Not only are exercises carried out to better advantage under water, but this treatment shares first place with occupational therapy in maintaining morale.

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Treatment.—Arsenical preparations were disappointing, both in the early and late stages. However, we had the impression that cases untreated initially were more prone

dysentery was observed in German prisoners of war in the Middle East by Spillane and Scott (1945). Similar cases have recently been seen in India in British and Indian troops returned from captivity.

HEAT STROKE

In India heat stroke was one of the principal medical causes of death amongst British other ranks. Improved methods of treatment have led to a lowering of the mortality rate, but as might be expected, some of the men who survived showed permanent sequelæ. The effects of heat stroke on the brain are at first generalized. On recovery from coma a variety of signs may be present, including severe mental confusion with incontinence, aphasia, pyramidal and cerebellar signs. As recovery proceeds the patient becomes orientated, ceases to confabulate, shows progressive improvement in memory, and is no longer incontinent. In short, the mental picture is very similar to that seen after a severe head injury. In a small percentage of cases this favourable course is not followed, a gross memory defect, both for recent and past events, persists and is accompanied by lack of interest, childish behaviour and incontinence. These signs of dementia vary in their severity and in the extent to which they eventually clear up. Inability to talk may be due to aphasia or to a gross dysarthria; both of these defects may be found in the same patient. Signs of a unilateral or bilateral hemiplegia clear up as a rule, although incompletely in some cases.

The most interesting sequel to heat stroke is a cerebellar picture. In July 1942 I examined three men in the Middle East who had recovered from heat stroke; all three were dysarthric and showed ataxia in their limbs, and unsteadiness in walking. None showed nystagmus. In two of these cases the signs cleared up in the course of a few weeks, but in the remaining case they persisted in association with signs of a gross dementia. In India I saw several similar cases, of which the following is an example:

Sergt. P., aged 40, on June 17, 1944, travelled 100 miles in a lorry west of Calcutta. He arrived at his destination in coma and was at once admitted to hospital where his rectal temperature was found to be 110°. Blood slides were negative for malarial parasites. He received energetic treatment for hyperpyrexia. On the evening of June 19 he recovered consciousness. He was moderately confused and incontinent. His speech was grossly dysarthric. He continued to improve slowly. On July 24 he appeared euphoric and showed involuntary laughter. He was well orientated and his memory was only slightly impaired for recent events. There was a rotatory nystagmus, especially to the right. Gross ataxia was present in both upper and lower limbs and he was unable to stand unsupported. The jaw-jerk was increased and there were signs of mild double hemiplegia. The picture he presented was very similar to that seen in advanced disseminated sclerosis. Two months later his condition was virtually unchanged.

Similar cases have been reported by Weisenberg (1912), R. M. Stewart (1918), and recently by Freeman and Dimoff (1944). Stewart postulated a cortical cerebellar lesion in his case and Freeman and Dimoff reported a case fatal on the third day in which changes in the cerebellum were maximal in the region of the Purkinje cells. Although in the case I have cited nystagmus was present, as a rule it is absent. Confirmation of a cortical cerebellar atrophy in these cases has been found by Major L. Krainer, R.A.M.C., a neuropathologist working in India.

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An Unusual Form of Epidemic Food-Poisoning with Neurological Symptoms

By DENIS BRINTON, F.R.C.P.

For thirteen months from October 1942 the population of Aden had been intermittently affected by epidemics of this food-poisoning. Perhaps 450 persons in all had suffered; and from the first (although the authorities did not learn this till much later) the natives had correctly blamed the Abyssinian wheat which had been shipped to Aden from the earliest harvest after the fall of the Italian East African territories, to save the better-quality Dominion-supplies, then very short for a number of reasons. According to the sufferers, this Abyssinian wheat was not only of poor quality, but contained a poisonous weed-seed, called in the local arabic *niscara*, literally to be translated as "tipsy", which you will see is a first-rate description of the effects it produces in man.

POLYNEURITIS

(a) *Diphtheritic*.—Several hundred cases of polyneuritis occurred in British and Dominion troops serving in the Middle East between 1940 and 1943. Nearly all of these cases were due to diphtheria. In India, diphtheria was uncommon during the war until the second half of 1944 when about 200 men of a special force employed in Burma were evacuated with polyneuritis which proved to be diphtheritic.

Both in the Middle East and India, approximately one-third of the cases were considered to be due to cutaneous infection. In cases with a cutaneous lesion and a history of a sore throat, it was not always easy to decide which was the focus of infection. If there was a history of paralytic throat symptoms then the case was considered faucial, but if such signs had never been present then an extrafaucial focus was presumed. Many cases of faucial infection were atypical either because of an associated streptococcal infection or because the throat signs were slight; consequently at times there were delays in administering serum, and this delay increased the risk of paralysis. Cutaneous infections were remarkable for their variety. The commonest lesion in the Middle East was the desert sore and in Assam and Burma its counterpart the jungle sore. Examples of polyneuritis were seen following a diphtheritic infection of a whitlow, scabies, an abscess, an infected in-growing toenail, and an infected hemorrhoid.

Diphtheritic infection of wounds was rare both in the Middle East and India. I have nothing to add to the excellent description of these cases given by Dr. Walshe in 1919 based on his experience in the M.E. during the first World War (1917, 1918). He divided the paralytic signs into local, specific and generalized. In a series of 30 cases of polyneuritis following skin infection he noted in 27% of these cases an onset of paralysis anatomically related to the infected focus. We have questioned many cases in this war as to whether the weakness began in the limb affected by the principal skin lesion, and have examined them from the point of view of an asymmetrical weakness corresponding to the infected limb, but the percentage of cases giving positive evidence of a local paralysis has been small. Localized numbness with or without sensory loss has been found somewhat more frequently. On the other hand, a certain number of typical cases of local palsy have been seen which support the general truth of Dr. Walshe's observations.

It is difficult to understand why paresis of accommodation, since it is a specific sign, should apparently be less common in extrafaucial as compared with faucial infection. An explanation may lie in the fact that following cutaneous infection there may be no local paralysis, and that a slight degree of paresis of accommodation, particularly in men engaged in active operations in the Field, may pass unnoticed or be forgotten by the time polyneuritic symptoms develop. Major A. D. Leigh, R.A.M.C., in an analysis of 100 cases of diphtheritic polyneuritis found that there was little difference in the incidence of paresis of accommodation in faucial and extrafaucial cases. With regard to treatment, in the early years of the war there was a tendency to immobilize severe cases in bed for weeks on end. Lieut.-Colonel Garland, R.A.M.C., who was in charge of a Neurological Centre in S. India, found that rapid improvement is possible, even in cases with gross postural loss, by means of exercises at first carried out in bed and later in a class under the supervision of a masseuse and P.T. Instructor. Since cases did not, as a rule, reach this centre for at least six weeks after infection, serious myocardial complications were not seen, and minor degrees of effort syndrome soon cleared up under this régime. No uncomplicated case of diphtheritic paralysis was evacuated to U.K. by this centre during 1944.

(b) *Nutritional*.—Polyneuritis complicating typhoid was occasionally seen. For example, in 1942 in one hospital in the Middle East I saw four such cases in which there was a history of prolonged fever and mental confusion which had led to difficulties in feeding. In two of these four cases, deafness preceded the onset of polyneuritic symptoms. In scrub typhus tenderness of the calves and feet is relatively common in severe cases, whilst a fully developed polyneuritic picture is not a rarity. The explanation is the same as in typhoid, namely inadequate feeding. In scrub typhus nerve deafness is common, but occurs independently of a polyneuritis. Several examples of Wernicke's encephalopathy were seen. The following is the history of one such case which I saw in the Middle East:

Lieutenant M., aged 29, was admitted to hospital on October 24, 1941, with infective hepatitis of one month's duration. Complete anorexia and frequent vomiting persisted after admission. The calorie intake was less than 500. On November 16 he complained of numbness round his knees. On November 27 double vision with a partial external ophthalmoplegia and nystagmus were noted. On December 2 he appeared emaciated and ill. There was no mental confusion. The ocular findings were confirmed. There was numbness with slight sensory loss on the feet. A diagnosis of Wernicke's encephalopathy was made. Treatment by daily injections of aneurin and additions to the diet resulted within a fortnight in rapid improvement in his general condition, cessation of vomiting, a return of appetite and disappearance of the eye signs; however, polyneuritic signs became more evident and persisted for some weeks.

A syndrome of great interest resulting from the association of a defective diet with

might also have been obtained. But hundreds of tons, not a few bushels, were needed; and primitive methods were totally inadequate to clean such quantities, even if the Ethiopian small-holder had somehow developed such an improbable concern for the fate of his brothers in Aden.

Nutritional Disorders of the Nervous System in the Middle East

By J. D. SPILLANE, M.D.

Nutritional polyneuritis.—In the Middle East during 1942-43 Polish troops and refugees filled some of the camps and hospitals of Paiforce and Palestine on their evacuation from Russia. Most of them had escaped into or had been transported to Russia in the winter of 1939-40. For two years they endured considerable hardships there and after the German invasion many of them were transported across the Caucasus to Iran, Iraq and Palestine. I had the opportunity of seeing many hundreds of these unfortunate people. Dysentery, malaria and typhoid were very common among them. Many were tuberculous. Malnutrition was widespread. Especially in the officer class one observed considerable loss of flesh; glossitis, œdema of the ankles, chronic diarrhœa were very common. A few had scurvy. Many of them had symptoms and signs of polyneuritis. Two types of case were encountered.

In the first and largest group symptoms dated back some six or twelve months. Difficulty in walking was the earliest complaint. Sharp pains in the soles of the feet and in the calf muscles would arrest progress and force the patient to rest—as in claudication. Affected individuals found difficulty in keeping their feet warm, painful dyæsthesiæ distressed them, especially at night. Muscle tenderness, wasting, weakness of the extensors of the toes and feet, sensory loss and reflex disturbances subsequently made their appearance in many cases. In the second group the onset of paralysis was quite rapid and almost always occurred during or shortly after an acute infective illness such as malaria, dysentery or typhoid. And yet I can say that I never once saw, during three years, a case of polyneuritis in a British soldier during such infections. Post-diphtheritic and acute infective polyneuritis were readily excluded in these Polish patients. A few fatal cases had terminal signs of brain-stem involvement—diplopia, ophthalmoplegia, paresis of the tongue musculature—and at post-mortem there were typical vascular lesions of the Wernicke type. But these hæmorrhagic lesions in the brain-stem were sometimes found where no localizing signs had been demonstrated ante-mortem (in some cases after careful observation).

On one occasion brief examination of the nervous system of all patients in one hospital ward revealed that about 25% had reduced or absent knee and/or ankle jerks. The majority were suffering from the acute infections of the type mentioned. I came to the conclusion that the neurological disturbance was one of nutritional polyneuritis. Many of them were already on vitamin-B therapy and one was able to watch the progress of nearly all of them (60 cases) during the following six to nine months. Thiamine when given intramuscularly seemed to improve appetite, relieve the sharp pains in the legs and feet and possibly increased the sense of well-being of some of the patients. But it had no effect whatever on the period of incapacity. Over and over again initial improvement of a subjective kind was thought to herald definite objective cure. Occasionally one observed some shrinkage of the area of sensory loss, but restoration of muscular power and reflex activity were never hastened. Yet these are the very signs which denote morphological alteration in the peripheral nerves and if consistently reversed would indicate some specific healing properties in the vitamin.

Since then I have had similar experiences with native and European prisoners of war and internees, in the Middle East and in the United Kingdom, and observation of over 200 cases of polyneuritis in these malnourished individuals has provided ample data on which the general effects of thiamine therapy may be judged. I have no strictly controlled series of cases to substantiate my conclusions—but they were never necessary. Routine clinical observation of cases which received adequate treatment with thiamine, by all channels, or who were given courses of treatment lasting one or two weeks (20 to 100 mg. daily), showed quite clearly that they fared no better than cases who received no additional supplements of vitamin.

On this problem of the "antineuritic vitamin" it seems probable that there is a large body of unpublished experience which indicates the inertness of vitamin B₁ in the treatment of polyneuritis. If general experience in the last ten years had established the value of thiamine we should not now have to debate the problem. The acceptance of liver and insulin therapy was never so long delayed, and there is no reason to suppose that a cure for polyneuritis will not be recognized when it appears. I do not think my clinical experience is necessarily in disagreement with the demonstration by the bio-

The natives insisted that this miscara was a common weed in every wheat-field of the Aden-peninsula also; and that, though they had never heard of any case of poisoning from the local crop, the greatest care had always been exercised by the farmers to remove the weed and its seeds from the wheat, at all stages from harvest to milling. In samples of Abyssinian wheat, they showed me how to recognize miscara, and in the hilum of many of these grains pointed to a black discoloration which under a hand-lens presented a mouldy appearance. Several samples of newly wharfed Ethiopian grain were collected and counted, and found to contain miscara-seeds in quantities up to 10%.

Reconstructing the clinical aspects of this food-poisoning by questioning both those who had suffered and the doctors who had had charge of them when ill (for the Governor had rightly frozen all stocks of the poisoned wheat a few days before I arrived, and the epidemics had come to an abrupt end), I learnt that, from one-quarter of an hour to two hours after taking food made of this grain, a man would become dizzy, and be smitten with headache, marked generalized tremors, lassitude, slurred speech, and a staggering gait. Sometimes, there had been vomiting and diarrhoea, and less commonly nausea and abdominal pain. Subsequent events seemed to vary directly with the amount of poison taken. If the subject had fed well, he paid for it by quickly subsiding into stupor or even a coma from which it might be impossible to rouse him for so long as ten hours; but, if he had taken only a little, his earliest symptoms would not noticeably increase and he might be fully recovered in three or four hours. There were no deaths, and within seventy-two hours even the most severely affected were well enough to resume their usual occupations.

Specimens of miscara sent home for botanical and chemical analysis revealed it to be a weed called the flax-darnel (*Lolium linicolum* or *temulentum*); and suggested that the poisonous element was in the mould to be seen on nearly every weed-seed, and was probably a pyridine-base of incompletely established chemical composition, known as temuline.

There were, however, certain paradoxes, necessarily slurred over in this bald statement of fact. First, it had to be established why Abyssinian wheat had proved poisonous to the inhabitants of Aden, though it had long been used in East Africa by the Italians, and more recently by us, without ill-effects. Secondly, I wished to find out how the natives of Aden came to have such an exact knowledge of miscara, although none could recall a case of poisoning from the local wheat, or indeed until the imports from Ethiopia began in 1942.

As to the first problem, a visit to a standard Italian mill in Eritrea provided the answer. Here, Ethiopian wheat, not less filthy, not less charged with miscara-seeds, was put through a complicated system of specially designed mechanical sieves before the wheat was milled. The resulting flour, long fed to the people of Eritrea and Abyssinia, was of course harmless; but Aden, without any sieving devices for cleaning the contaminated grain, had milled miscara with wheat and become poisoned.

As to the second paradox, the only explanation was the traditional usages of the small farmers of the Aden protectorates. No case of miscara-poisoning from locally grown wheat could be recalled, merely because from time immemorial scrupulous attention had been paid to the removal of the weed and its seeds from the harvested wheat. The miscara-plant, they said, is easily identified from the time when the crop has grown to a height of about one foot; it is a darker green than the wheat, and splits a short distance above the ground into five or six heads. Before the crop is cut, which in these extremely primitive communities is done by grasping a stool of stalks and severing them near their base with a curved knife, as much miscara as possible is weeded out; but some is unavoidably cut with the wheat, and is spread out with it in a clean place to dry in the sun. When these products of the harvest are dry, most of the grain is removed by a heavy stone drawn by oxen. Afterwards, what remains attached is hand-picked from the stalks, and all the free grain is then winnowed and housed. As wheat is required for food, the women take the grain from store and once more spread it in the sun. After it is warm, it is tossed up again and again in a straw-basket, so that light impurities such as husks are blown away. The same process flicks most of the miscara-seeds to the edge of the basket, whence they are readily removed. The residue is finally hand-picked, grain by grain, until all dirt, miscara-seeds, and other foreign bodies are separated. With these precautions, clearly applicable only to small holdings, local wheat can always be eaten with safety.

So, in essence, these epidemics of food-poisoning arose from the wartime marriage of primitive methods of agriculture to modern methods of distribution. If the Abyssinian harvest had been put through modern threshing machines, with their ordered winnowing arrangements, no seeds smaller than mature wheat-grains would have been exported to Aden, and the seeds of the flax-darnel would have been excluded. If the project could have been on a small enough scale to allow the hand-picking just described, clean wheat

none other than acute Wernicke's encephalopathy. Some authorities consider that breast-milk intoxication is a special variety of infantile beriberi.

In the German cases pellagra and ariboflavinosis were *not* present when they were under observation and only a few gave a history of such affections. Treatment was largely unsuccessful in clearing up the neurological signs. There was subjective improvement but the number which showed objective relief was small. Yeast, liver, nicotinic acid, riboflavine and thiamine were freely used for long periods.

ÆTIOLOGY

Vitamin A.—It has not been shown that vitamin A is concerned with the functioning of the nervous system. The nervous lesions in growing animals deprived of the vitamin are mechanical in origin. Blindness, deafness and ataxia have been satisfactorily explained on the basis of disproportionate growth of the nervous and skeletal systems (Mellanby, 1940; Wolbach and Bessey, 1941). The cranial and spinal cavities are underdeveloped and overcrowded.

Lathyrism, a few cases of which I saw in Syria, has also not been clearly related to deficiency of this vitamin, and there is some doubt about the nature of follicular hyperkeratosis and its deficiency ætiology (Stannus, 1945).

Vitamin-B complex.—Here we are on surer ground. I shall not go into the controversial aspects of the experimental evidence which indicates that some factors, at least, of the vitamin-B complex, are necessary for the normal activity of the central and peripheral nervous system. Chronic mild thiamine deficiency can give rise to degeneration of peripheral nerves (Swank *et al.*, 1940, 1941, 1942) in animals. Reduction of visual acuity (Peters, 1934, Marchesini, 1935) and deafness (Selfridge, 1937, Covell and Noble, 1937, and Covell, 1940) with degeneration of the optic and cochlear nerves has been demonstrated in thiamine deficiency. The posterior columns of the spinal cord may be affected (Zimmerman, 1941) and lesions identical with those found in Wernicke's encephalopathy can be produced with significant regularity by thiamine deficiency (Prickett, 1934; Alexander *et al.*, 1938, 1940) in pigeons, fish and foxes. In man experimental thiamine deficiency (Williams *et al.*, 1939, 1940, 1941 and 1943) produces a condition of a "neurasthenic" kind with but little evidence of polyneuritis, but in some cases flaccid weakness of the leg muscles and loss of the knee-jerks may develop and painful sensory disturbances in the lower limbs may be manifest (Jolliffe *et al.*, 1939).

Deficiency of riboflavine in experimental animals produces symptoms and signs, which as in the case of thiamine, vary according to the acuteness of chronicity of the condition. Acute deficiency produces collapse, after an interval of 100 to 150 days in dogs, and death will result if there is not prompt administration of the vitamin. These animals fail to show definite neurological lesions of a specific nature. In chronic deficiency there is ataxia and loss of tendon-jerks and at post-mortem there is degeneration of peripheral nerves and of the posterior columns of the cord (Sebrell *et al.*, 1937, 1938; Zimmerman *et al.*, 1941; Phillips and Engel, 1938; Lightner and Forbus, 1940, and others).

Isolated nicotinic acid deficiency in animals has been little studied but spinal cord lesions of moderate degree have been observed (Zimmerman, 1941). In pyridoxine B_6 deficiency severe anaemia and epileptiform attacks have been described and there are degenerative changes in the peripheral nerves and posterior columns of the cord (Wintrobe *et al.*, 1938, 1942 and others). Pantothenic acid is thought to be essential in the preservation of the spinal cord in chicks (Phillips and Engel, 1939). However, there are no indications that similar disturbances arise in man as a result of deficiency of pyridoxine or pantothenic acid.

There is plenty of clinical evidence which indicates that lack of the B complex, in whole or in part, leads to disturbances of the nervous system.

Retrolubar neuritis is found in pellagra, beriberi and in association with ariboflavinosis. Of 57 British P.S.O.W. from the Far East whom I have recently seen, no less than 45 had had beriberi. There were complaints of loss of vision in 35 (not due to refractive errors) and in 17 there were residual central scotomata. In Japan, retrolubar neuritis in men is nearly always seen in association with mild chronic beriberi, rarely in the acute form. In women it is almost invariably associated with lactation (Kagawa, 1938). There is a Japanese proverb which advises lactating women against sewing with a needle as it is a strain on the eyes at such times. Kagawa mentions a type of case seen in Japan, among individuals who have had several attacks of beriberi, in which retrolubar neuritis, nerve deafness and tinnitus, and ataxia are combined. He thought they were a special form of beriberi, in which peripheral paralysis was largely replaced by sensory ataxia. Thiamine cured them if the condition was not chronic. Retrolubar neuritis is also found in Wernicke's encephalopathy, and in hyperemesis gravidarum, with or without polyneuritic or encephalopathic signs.

Deafness is uncommon in beriberi but is mentioned by many of the older writers as occurring frequently in pellagra. It has been noted in patients suffering from

chemists that thiamine is concerned with the metabolism of the nervous system. The relief afforded by thiamine of the opisthotonus of the B₁ deficient pigeon is explicable only on the basis of a reversible biochemical lesion. But no such state has been observed in human polyneuritis. Acute beriberi in the infant and adult is essentially a cardiac disturbance. But that dramatic recovery from acute lower motor neurone paralysis *can* occur in man is well shown in the instances of tick paralysis following removal of the tick, and in myasthenia gravis and periodic paralysis on the administration of prostigmin or potassium respectively. Here we have evidence of reversible biochemical disturbances affecting the nervous system. But in human polyneuritis dramatic recovery does not occur and the pathological evidence points, not to the nerve cell or neuromuscular endplate, but to the peripheral axone as the site of injury. If a biochemical disturbance resulting from B₁ deficiency were the cause of polyneuritis should we not be justified in expecting better results than are generally achieved by the use of thiamine? One can only conclude that the relationship between the *biochemical* lesion of experimental B₁ deficiency and the *morphological* lesions of polyneuritis has yet to be demonstrated.

Perhaps we should recall the analogy made many years ago by Wright (1903) when he pointed out how misleading would be our conception of diphtheria if we based our studies of its pathology on post-diphtheritic polyneuritis. Most accounts of the pathology of beriberi are based mainly on chronic beriberic polyneuritis—which may well be in the nature of a residual phenomenon. Beriberi is certainly much more than polyneuritis and to consider these diseases as identical—with alcohol, white bread and breakfast cereals playing the role in the West that is taken by rice in the East—is a conception which is not altogether satisfactory.

A NEUROLOGICAL SYNDROME IN PRISONERS OF WAR

A neurological syndrome appeared in a German P.O.W. camp in the Canal Zone and the condition also occurred in other camps, in one of which it was widespread. The German camp housed soldiers of the Afrika Korps who were captured after the Battle of Alamein. Dysentery, infective hepatitis, malnutrition, œdema of the limbs were common among them at the time of capture. Many developed polyneuritis and an outbreak of pellagra occurred in the camp in December 1942. Thereafter pellagra was uncommon and beriberi did not arise. The mucocutaneous manifestations of riboflavin deficiency were not commonly observed. Diarrhœa and dysentery, however, remained a source of trouble during the next three years. In August 1943 the first cases of the neurological syndrome began to appear. They cropped up—a few each month—until, by January 1945, there were over a 100 at this camp. The distinctive features of the syndrome were retrobulbar neuritis, nerve deafness and ataxia. Other disturbances were laryngeal paresis, trigeminal hypoalgesia, loss of the senses of taste and smell, a mild secondary anaemia and reduction of free gastric HCl. Some cases showed cutaneous lesions of the lower limbs of the type known as follicular hyperkeratosis. But these disturbances were not common. More than half the total number of cases developed the ocular manifestations only—failing vision, central scotomata and, eventually, pallor of the optic discs. In about 20% there was some reduction of hearing, a few were very deaf. Painful dysesthesia of the lower limbs was a striking complaint in about 30%; half of these became ataxic. In such cases there was gross disturbance of stance and gait, retention of almost normal power in the legs, exaggerated tendon reflexes and loss of deep sensibility. In a few long-standing cases the ankle-jerks were reduced or lost and there were signs of slight involvement of the peripheral nerves. Superficial sensory loss was never marked and at no time were extensor plantar responses observed. The abdominal reflexes remained brisk and the arms were rarely affected. Outwardly, with a few exceptions, these men looked quite fit. By ordinary standards one would not have said they were malnourished, but I satisfied myself that their rations were seriously defective and that failures of supply, the substitution of alternative items of low vitamin content and primitive cooking arrangements were largely responsible for the deficiencies. Chronic diarrhœa, which was widespread in the camp, no doubt aggravated the condition.

One important case was that of a man who went ill with an attack of generalized œdema. A few weeks later he developed the typical picture of Wernicke's encephalopathy and responded quite remarkably to thiamine intramuscularly. But he was left with retrobulbar neuritis, nerve deafness, altered voice and ataxia. He actually developed a marked degree of polyneuritis when on treatment. I understand similar cases of Wernicke's syndrome have been observed in British P's.O.W. in the Far East, many of whom died and at post-mortem showed the characteristic brain-stem lesions. I have seen some of those who probably developed this syndrome in the East and who have residual signs of polyneuritis with or without visual reduction from retrobulbar neuritis. Wernicke's syndrome has not figured in the accounts of vitamin-B deficiency states described in Japan and elsewhere in the Far East, but Tanaka in 1943 came to the conclusion, from clinical and pathological investigation, that so-called breast-milk intoxication in Japanese infants was

none other than acute Wernicke's encephalopathy. Some authorities consider that breast-milk intoxication is a special variety of infantile beriberi.

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so-called acute nicotinic acid deficiency encephalopathy and in the polyneuritis associated with pregnancy.

A hoarse, weak voice is rare in pellagra but very common in beriberi. In the infantile form it is said to be pathognomonic and on many occasions has been shown to be due to recurrent laryngeal nerve paralysis; others attribute it to oedema of the larynx. In acute polyneuritic beriberi of adults it has also been observed (Jacob Bontius described it in 1645) and many prisoners of war in the Far East were so affected. Nine of my patients lost their voice during severe bouts of beriberi and many had hoarse weak voices for six months or more. A few have permanent changes. This disturbance has also been noted in association with polyneuritis during pregnancy.

Stannus (1944) has drawn attention to the possibility of deficiency of riboflavin or some allied substance as of aetiological significance in these nutritional affections of the nervous system. They have frequently been noticed in association with the mucocutaneous manifestations of riboflavin deficiency, with and without coexistent signs of nicotinic acid deficiency. It was interesting to learn that scrotal dermatitis due probably to riboflavin deficiency was very common among the P.O.W. group from the Far East. 46 out of 57 of my cases had intolerable itching, weeping and sometimes excoriation of the scrotum.

These random observations serve to indicate the complexity of the problem as to which particular member of the B complex is largely concerned with the production of these disturbances. It is very easy to follow only one track and perhaps no useful purpose is served in any attempt to classify them on the basis of existing knowledge. Some of these lesions were noted by the older pellagrologists in that hybrid affection we call pellagra. Even the recent accounts of acute nicotinic acid deficiency encephalopathy read very similarly to some of the old accounts of "typhoid pellagra". As Lombroso said of pellagra, "There is no disease, only the diseased".

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A Central Nervous Deficiency Syndrome

By HUGH G. GARLAND, T.D., M.D., F.R.C.P.

IN February 1942 a number of British and Indian troops were captured by the Japanese and interned in Rangoon Gaol. They were released in April 1945 and, after rapid medical examination in India, were returned home. It was not at first appreciated that a number of these men showed an interesting neurological syndrome, but eventually I had the opportunity of examining 8 such cases. Later in the year Spillane and Scott (1945) recorded a series of 107 cases of a similar nature recognized by them in the Middle East in 1944, these being German prisoners.

After being incarcerated for a period, which in my cases was not less than eight months, defects of vision, hearing and gait develop. Of these the defect of vision is the only constant feature, commencing with failing vision, particularly near vision, which increases for weeks or months and then remains stationary, no case proceeding to complete blindness. Examination at this stage shows a very striking bitemporal pallor of the optic disc in most cases, and probably in every case there is some defect

of central vision. This defect is usually only demonstrable on a 2-meter screen, ordinary perimetry often showing no abnormality. The scotomata are central or paracentral, relative or absolute, for white or for colour. The defect of hearing consists of bilateral nerve deafness with or without tinnitus and, though sometimes severe, never proceeding to complete deafness. Symptoms referable to the spinal cord consist of numbness and tingling in the legs, rarely in the hands, and in the more severe cases unsteadiness of gait. The most constant objective finding is loss of vibration sense, frequently from the pelvis downwards, and in some there is loss of postural sense in the toes. There are considerable variations in the knee and ankle jerks, some being brisk, others absent. In one of my cases there were double extensor responses and in two others the plantar responses were equivocal. These are the essential features of the syndrome, though Spillane and Scott also noted laryngeal palsies and mental deterioration. In one of my cases, the most severe in all respects, there was intellectual deterioration with behaviour disorders. Within the past week, through the kindness of Mr. George Black, I have seen two further cases; one of these had also been in Rangoon Gaol and the other had been interned for a similar period in Hong Kong. Of the 10 cases I have examined, 6 were English, 1 Anglo-Burmese, and 3 Indian (2 Churkas and 1 Rajput). Vision was affected in all cases; the spinal cord in 6 and hearing in 4. All these 10 had been essentially on the same diet, and all had lost two or more stones in weight. In no case was there any history of glossitis, angular stomatitis, or scrotal dermatitis nor had any of them suffered from malaria, dysentery or other notable disease. Further investigation gave largely negative results, in all cases the spinal fluid being normal, gastric secretion being within normal limits, and the blood picture showing nothing more than a simple anaemia with eosinophilia, no doubt associated with hookworm infestation, which was present in them all. All these features have already been described by several authors and the only new clinical observation I made was that of continuous and rapid nystagmus in one man.

It would seem a reasonable assumption, requiring no further discussion, that this disorder is neither hereditary nor infective, but is almost certainly degenerative. Two factors might underlie such a degenerative process; one a toxin, such as that which causes lathyrism, the other some dietary deficiency. The toxic theory can, I think, be dismissed as being highly improbable in view of the fact that the syndrome has been observed in a wide variety of races scattered over Europe and Asia. Although most of the recorded cases have occurred in prisoners, the only feature common to all is that the victims have been living for a long period on a deficient diet.

Spillane and Scott considered the possibility of their cases resulting from alcohol, but this can be ruled out in my series as not one of these cases had taken alcohol in any form during the relevant period. Their final conclusion was that they were dealing with a nutritional neuropathy, the exact factor responsible being unknown. Unfortunately Spillane and Scott were only able to say what their cases should have been eating, and made no reference to what they did in fact eat, either in terms of calories or of the type of food. The diet their cases should have received was of a standard that, Dr. F. C. Happold tells me, was achieved by few people in this country throughout the war, with the possible exception of a few workers in the heaviest industries. That the cases of Spillane and Scott were not receiving the dietary laid down is implicit in the fact that from the camp in which cases had developed their neuropathy there were large numbers of cases of scurvy, beriberi and pellagra. I am more fortunately placed in that I know, more or less exactly, what my patients were eating. During the whole period they were given no bread, milk or butter. The basis of their diet was parboiled rice, about three-quarters of a pound per day, served in two or three meals. Meat was limited to two small pieces per week, the meat being very lean and often decomposed. It was usually buffalo, sometimes beef, and occasionally pork, but in all cases it contained practically no fat. Vegetables were eaten two or three times a week in the form of pumpkin, marrow, cabbage and chrysanthemum leaves, with occasional onions. Most of them received the grains dhal or gram daily and these, as with all the vegetables, were boiled. Small quantities of boiled sweet potato were served daily. During the first year limes or a banana were issued once a week and for the greater part of the time raw cucumber was available. The average egg ration was one or two a month. There was a small ration of tea and sugar, and the salt intake was adequate. Some of the men were able to smoke cheroots, but this was inconstant and in no case excessive. My first impression was that this diet might be deficient in vitamin A, as it contained little animal fat and the green vegetables, such as cabbage and chrysanthemum leaves, that were issued, were usually more yellow than green and often several days old. I was also reminded of the work of Mellanby (1931) in which an almost identical syndrome was produced in young animals living on a diet deficient in vitamin A only. It is now, however, thought that the neural changes in these animals resulted from the pressure of hypertrophied bone. Dr. Happold has studied the diet I have described and feels that vitamins A, B₁,

so-called acute nicotinic acid deficiency encephalopathy and in the polyneuritis associated with pregnancy.

A hoarse, weak voice is rare in pellagra but very common in beriberi. In the infantile form it is said to be pathognomonic and on many occasions has been shown to be due to recurrent laryngeal nerve paralysis; others attribute it to oedema of the larynx. In acute polyneuritic beriberi of adults it has also been observed (Jacob Bontius described it in 1645) and many prisoners of war in the Far East were so affected. Nine of my patients lost their voice during severe bouts of beriberi and many had hoarse weak voices for six months or more. A few have permanent changes. This disturbance has also been noted in association with polyneuritis during pregnancy.

Stannus (1944) has drawn attention to the possibility of deficiency of riboflavine or some allied substance as of aetiological significance in these nutritional affections of the nervous system. They have frequently been noticed in association with the mucocutaneous manifestations of riboflavine deficiency, with and without coexistent signs of nicotinic acid deficiency. It was interesting to learn that scrotal dermatitis due probably to riboflavine deficiency was very common among the P.O.W. group from the Far East. 46 out of 57 of my cases had intolerable itching, weeping and sometimes excoriation of the scrotum.

These random observations serve to indicate the complexity of the problem as to which particular member of the B complex is largely concerned with the production of these disturbances. It is very easy to follow only one track and perhaps no useful purpose is served in any attempt to classify them on the basis of existing knowledge. Some of these lesions were noted by the older pellagrologists in that hybrid affection we call pellagra. Even the recent accounts of acute nicotinic acid deficiency encephalopathy read very similarly to some of the old accounts of "typhoid pellagra". As Lombroso said of pellagra, "There is no disease, only the diseased".

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A Central Nervous Deficiency Syndrome

By HUGH G. GARLAND, T.D., M.D., F.R.C.P.

In February 1942 a number of British and Indian troops were captured by the Japanese and interned in Rangoon Gaol. They were released in April 1945 and, after rapid medical examination in India, were returned home. It was not at first appreciated that a number of these men showed an interesting neurological syndrome, but eventually I had the opportunity of examining 8 such cases. Later in the year Spillane and Scott (1945) recorded a series of 107 cases of a similar nature recognized by them in the Middle East in 1944, these being German prisoners.

After being incarcerated for a period, which in my cases was not less than eight months, defects of vision, hearing and gait develop. Of these the defect of vision is the only constant feature, commencing with failing vision, particularly near vision, which increases for weeks or months and then remains stationary, no case proceeding to complete blindness. Examination at this stage shows a very striking bitemporal pallor of the optic disc in most cases, and probably in every case there is some defect

Section of Anæsthetics

President—GEORGE EDWARDS, M.R.C.S., D.A.

[December 7, 1945]

Sepsis and Asepsis in Spinal Analgesia

By FRANKIS T. EVANS, M.B., D.A.

SPINAL analgesia has its place in anæsthetics, and under certain conditions is the method of preference. Though meningitis has occurred on certain occasions following its use, let us remember that many, many thousand spinal anæsthetics have been given without incident. During the twenty years I have been at Bart's Hospital I have not known of any case of meningitis in that hospital following spinal anæsthesia. Similarly, during the ten years I have been at St. Mark's Hospital there has been no meningitis in 2,500 spinal anæsthetics.

To condemn a useful and well-trying method because of a small proportion of unfortunate happenings in a vast total of cases is wrong. Yet we should inquire into those cases in which sepsis has occurred and endeavour to discover the cause. This is no easy task, for the reaction varies, from the so-called aseptic meningitis in which no organisms have been demonstrated, to a frank purulent meningitis due to a proven organism. Some of the meningitis cases recorded have shown some very unwelcome symptoms in that they have been prone to relapse.

There are many points at which the technique of spinal puncture can break down. In the past the methods of sterilization of apparatus have varied enormously, and this question of sterilization is of more than technical interest, for it has now a medico-legal aspect.

A report has recently been issued through a committee appointed by the Medical Research Council with regard to the sterilization of syringes. This committee consists of men whose opinions and recommendations carry weight. It is possible that a practitioner might be faced with this report by cross-examining counsel, and he might well find himself in an awkward predicament if his apparatus had not been sterilized in accordance with the recommendations laid down in this report.

Sepsis can enter the spinal canal as a result of spinal puncture:

- (1) From the hands of the anæsthetist.
- (2) From the skin of the lumbar area.
- (3) From the imperfect sterilization of syringes and needles.
- (4) From contamination of needles and syringes, which may occur through: (a) Infection from imperfectly sterilized towels; (b) Infection from so-called sterile water or sterile distilled water; (c) Infection from the local anæsthetic solution—novocain; (d) Infection from the spinal drug.

(5) Infection may also occur from hæmatoma due to repeated attempts at spinal puncture. Mr. Rogers tells me of cases within his knowledge where sepsis occurred as a result of hæmatoma due to repeated attempts at spinal puncture. A younger colleague has given me particulars of one case when a certain assistant anæsthetist was deputed to perform a spinal anæsthetic. He made several attempts to enter the spinal canal but failed. His chief then arrived and performed lumbar puncture at the first attempt in the space above. At the site of the assistant anæsthetist's many punctures, the patient subsequently developed an extradural abscess which spread subdurally. The patient died of meningomyelitis due to *Staphylococcus aureus*. The apparatus used for the puncture by both anæsthetists was autoclaved. It is significant that the assistant anæsthetist did not wear gloves.

With regard to the hands of the anæsthetist, I know that it is possible to perform a lumbar puncture without scrubbing up, and that it is equally possible to put on a pair of sterile rubber gloves without washing up and without contaminating the gloves. But the wisest course is to scrub the hands with soap under running water, just as one would do for any other surgical operation. The hands should then be well rinsed in 95% or 70% spirit, preferably for two minutes, and be allowed to dry. If the spirit is not allowed to evaporate from the hands, they should be dried with a sterile towel. Furthermore, I would recommend the use of sterile rubber gloves put on in the proper manner. If all these precautions are observed, the anæsthetist may be pretty sure that no infection can be conveyed from his own hands.

Skin preparation.—Obviously, no one would perform a spinal if the skin of the lumbar area were covered with acne or any infectious skin lesion. Professor Garrod

riboflavine and ascorbic acid, would be present in adequate amounts, though the nicotinic acid content is doubtful owing to the unknown composition of the cereals.

An allied syndrome was well described by Landor and Pallister (1935) in civilian Chinese, Malays, and Indians, in gaol in Malay. In all their cases, the neuropathy was preceded by glossitis, angular stomatitis and scrotal dermatitis. They did not describe deafness. The number of affected persons varied from 2 to 7% of the inmates (the incidence in Rangoon Gaol was probably 5 to 10%); there was no evidence of beriberi in the prison and they attributed the disorder to deficiency of vitamin B₂, claiming that the early symptoms responded rapidly to marmite or yeast and more rapidly still to liver treatment. Among American internees in Manila Whitacre (1944) described paresthesia and difficulty in focusing the eyes, which he regarded as due to vitamin B₂ deficiency, but the clinical descriptions are inadequate and he may not be describing the same disorder. Wilkinson and King (1944) have observed a similar condition in the civilian population of Hong Kong in 1940, at a time when pellagra became prevalent for the first time; there was no evidence of glossitis or stomatitis, but they regarded it as due to a dietary deficiency, considered that it was a form of pellagra and claimed results from nicotinic acid treatment. The diet in their cases was almost identical with that of my patients. Adolph and others (1944) described visual failure in American civilian internees in Japanese hands; there were associated cases of beriberi and pellagra and they felt that there was no evidence of deficiency of vitamins A, C or D. They claimed some improvement from yeast, but thought that the syndrome could not be related to any specific defect of diet and claimed no results from thiamine, nicotinic acid or riboflavin. Similar cases were also observed amongst civilians during the Spanish civil war in 1937-38, and in the past few weeks many more cases have appeared in this country, following imprisonment in Singapore, Java, and other places.

Reviewing the recorded cases, the following features therefore emerge. A clear-cut neuropathy has developed in a variety of races, scattered over the Middle East, the Far East and Spain. Although most of the victims have been in prison, the one factor common to all groups has been a defective diet. Although in all cases vitamin intake must have been low, and in many cases classical syndromes of vitamin deficiency have co-existed, there is no clear proof that this disorder has resulted from deficiency of any known vitamin. There has almost certainly been no deficiency of vitamins C or D and probably not of A. In my own cases, as well as in some of the others, the neuropathy has developed in the complete absence of any of the classical symptoms associated with deficiencies of any of the known members of the B group. At the same time, the indications generally point to the B group as the probable source of deficiency, and it seems probable that the deficiency is to be found here and that it may even be a deficiency of some member of this group at present unknown. Stannus (1944) regarded this syndrome as being probably the result of hypo-riboflavinosis, but certainly in my cases there is little evidence to support this view. The observation of this syndrome is relatively new but it is probable that in the past it has been missed or mistaken for something else; for example, it may well account for cases of optic atrophy and other unusual findings which have from time to time been reported as variants of both beriberi and pellagra. My own cases had in fact been seen by several physicians and variously ascribed to neuro-syphilis or to optic atrophy possibly the result of tobacco. I have little doubt that the prison populations of the tropics contain many more examples of this deficiency, which can be by no means rare, and an examination of such communities probably offers the most helpful field for future research. In the meantime the number of affected ex-prisoners now in this country has probably reached hundreds, possibly thousands. At present there is no known therapy of proved value and it would appear probable that some of the changes are irreversible. At the same time therapeutic possibilities in long-standing cases are not yet exhausted. We are all familiar with the optic atrophy and failing vision which sometimes complicate subacute combined degeneration of the cord. Remarkable recovery of vision may occur following liver therapy in this condition, and the changes in the spinal cord in this disease are by no means irreversible. There appears to be varying degrees of improvement in hearing following the return to a normal diet, but I am not aware of any improvement in vision nor of any change in the spinal cord dysfunction. I feel that this neuropathy is a discovery of considerable importance, that it is probably quite independent of beriberi and of pellagra, and that further investigation of its aetiology should be carried out at the source.

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My own preference for sterilizing all-glass syringes is boiling in distilled water in a small sterilizer, and I prefer to boil them myself and dish them up myself, picking them out of the sterilizer (which is fitted with a rising tray) with my gloved hands.

There are other possible ways in which infection may occur. I know of one case in which pyocyanus meningitis occurred, the only possible failure in technique apparently being that the trolley was not covered with a sterile mackintosh under the sterile towel. The towel became sodden with water when the syringes were dishd up and it is presumably possible that contamination arose through the towel.

The rinsing of spinal syringes with so-called sterile distilled water has caused several cases of meningitis. Wilson Smith, Professor of Bacteriology at Sheffield, examined the sterile distilled water of several hospitals. Of 223 examinations of cerebrospinal fluid and water he was able to grow water-borne non-pathogenic organisms from 89; and from sterile distilled water he could grow organisms after the bottle had been opened for a few hours. Cuthbert Dukes grew a pure culture of pyocyanus from a sample of cerebrospinal fluid sent for examination and from distilled water. The cerebrospinal fluid was otherwise normal, and the patient showed no sign of meningitis. The real culprit was discovered to be the sterile distilled water in which the syringe and needle had been rinsed before use. This water came from a winchester of sterile distilled water which had already been opened. The remedy is obvious: if you must rinse your syringe and needles in sterile distilled water, take it from a new bottle which has been freshly sterilized. Barrie (1941) was using water from a Berkefeld filter which was defective, and although the organisms grown from the water were non-pathogenic, nevertheless when they ceased rinsing their syringes in this water the outbreak of meningitis following spinal anaesthesia ceased.

I know of an outbreak of meningitis following spinal anaesthesia in which the infecting organism was *B. coli*. Pyocyanus and *Staphylococcus aureus* have been grown from the cerebrospinal fluid and from the local anaesthetic used. I have, however details of one case which occurred after spinal puncture, the infecting organism here being *Staphylococcus albus*. It is interesting to note that symptoms did not occur until nine days after the operation, when the patient complained of a slight headache and vague pains over the coccyx and sacrum on getting up. He became pyrexial next day, but there was no definite sign of disease although he was examined by a medical specialist three days later. Eventually he was lumbar punctured some four days after that, i.e. eighteen days after the operation. The fluid withdrawn was opalescent and showed a lymphocytosis. The culture proved sterile. The next day he developed meningeal signs and was lumbar punctured again, the culture again being sterile.

Two days after this the lumbar puncture produced a growth of *Staphylococcus albus* on culture. He died on the following day. By this time the cerebrospinal fluid showed polymorph cells as well as lymphocytes. Sulphadiazine proved ineffective although given intravenously in a continuous drip. At post-mortem the extradural space was filled with blood-stained purulent fluid. The subdural space contained a little thin, cloudy fluid, and the subarachnoid field had thick pale-yellow pus extending throughout the length of the cord, most marked at the lower end. The spinal cord appeared to be normal. It was interesting to note that although the dura had been punctured on three separate occasions there was only one puncture hole to be seen.

The technique of lumbar puncture in this case was as follows: all-glass syringes, kept separately and used only for spinal anaesthesia; Howard-Jones needles; all apparatus boiled for twenty minutes. The local anaesthetic was 2% novotox from a freshly autoclaved bottle. This same local anaesthetic was used for other patients on the same day with no ill-effects.

The two cases of pyocyanus meningitis which occurred in a certain hospital where I worked I have already published, but there are one or two interesting points with regard to them. First, they both died and it was only after some three days had elapsed that there was any suggestion that meningitis had been present. Both patients were drowsy and complained of headache and rigidity of the neck. Both died comparatively suddenly and the course of the illness was afebrile. In the one case there was a generalized meningitis with thick pus up to the base of the brain, but pyocyanus was present in the turbid cerebrospinal fluid. In the second case the picture was complicated by the fact that the patient had a large retroperitoneal hæmorrhage which I suspect was the real cause of death.

The technique employed with these two patients was as follows. The spinal syringes were of the Record type and were kept by themselves in industrial spirit and used solely for spinal analgesia. They were rinsed with sterile normal saline together with the needles, and the skin was prepared with iodine and spirit, the anaesthetist wearing gloves. The local anaesthetic in both instances was novocain from a rubber-capped

told me that *B. coli* and *B. welchii* had been cultivated from the lumbar skin (R. A. Shabter). He thinks that it is more than probable that the lumbar skin becomes contaminated from the anus as a result of wearing pyjamas. It is also possible for organisms to be carried in by the needle, either on the point or just inside the lumen of the point. For this reason some people recommend an introducer, like the Sise introducer. On the other hand, there is the possibility of the organisms being wiped off as the needle advances in the ligamentous structures.

The literature on skin sterilization is voluminous. Personally I like old friends, and I pin my faith to soap and water first, this being followed by tincture of iodine and then spirit. My authority for this is Professor Garrod in a personal communication, and the work done by Hatfield and Lockwood whose test methods were first class and who proved to their satisfaction that iodine and spirit were highly efficient. They performed a series of experiments which were both simple and ingenious. They tested a series of skin disinfectants and were disappointed with the efficacy of the mercury preparations. They found that 95% alcohol applied to the hands for two minutes after scrubbing with soap and water proved the most effective skin preparation for the hands of personnel, but that if this was too expensive 70% alcohol was almost as effective. Alcohol, unlike CTAB, is, of course, not affected by soap.

Hatfield and Lockwood also found that for disinfection of the patient's skin 3-5% tincture of iodine, allowed to dry and followed by alcohol, which in turn is allowed to evaporate, was superior to other methods, and for this reason I remain loyal to iodine and the industrial spirit.

Although it is possible for infection to be carried in from the surface layers of the skin, I believe that meningitis, when it occurs, is introduced through the lumen of the exploring needle owing to an error in technique.

Sterilization of syringes and needles.—The report from the committee appointed by the Medical Research Council, dealing with the sterilization of syringes, recommended that syringes for spinal analgesia be all-glass and not glass and metal, for in the latter type of syringe infected clot or organisms can lodge in the interstices of the cement into which it is very difficult for the sterilizing fluid to penetrate. This committee suggests that the best method of sterilization for needles and syringes is either by dry heat at 160°C. for one hour (the thermometer being near the syringes), or by autoclaving at 120°C. for twenty minutes at 15 to 20 lb. pressure. The former of these methods is definitely inimical to the Record syringe, and the second is often so, as the temperatures are such as to melt the cement. For this type of sterilization one must therefore have glass syringes.

For years I put my syringes, taken apart, together with the needles (run through with spirit) into ordinary industrial alcohol for some ten to fifteen minutes before use. Fortunately nothing went wrong. Then I took to keeping them in industrial spirit in an airtight case. I had no cases of meningitis, and I personally have been fortunate in that I have never had a case of meningitis. The reason, I think, was due to the fact that those syringes and needles were used for nothing but spinal punctures.

I have seen syringes taken from a jar of spirit and placed ready for spinal anaesthesia. In that jar were other syringes and needles used for exploring and for aspirating pus. This practice cannot be too strongly condemned. Only the other day I saw a nurse preparing a trolley for a spinal anaesthetic. She took a syringe from a jar of spirit in which were other syringes, one of which had only been returned to the spirit some five minutes earlier. She placed the syringe in a sterile bowl and then went to the tap and ran tap-water into the bowl in order to rinse out the spirit.

The Medical Research Council Committee tells us that 90% industrial spirit will kill organisms (according to their experiments) in twenty-two minutes, and that 70 to 75% alcohol kills vegetative organisms in a much shorter time. They agree to the use of this method where the other methods are impracticable. They suggest that all-glass syringes be used and that they be immersed in 70 to 75% spirit for five minutes. The spirit must be fresh. Apparently organisms are killed by spirit but not spores; hence the emphasis on fresh spirit. (To make 70 to 75% spirit take four parts of industrial alcohol and one part of water.)

The Medical Council state that if dry heat or autoclaving is not possible, then boiling for five minutes in water is reasonably safe. I would add to that and say boil for five minutes in distilled water, for if the water in which the syringes are boiled is alkaline there is a risk of precipitating the anaesthetic as its insoluble base. Needles, too, may be boiled, and if fitted with guards they do not lose their sharp points.

The use of boiling oil for sterilization of syringes, although reminiscent of Gilbert and Sullivan, is not recommended for syringes, as the results are not uniform, although this method is quite satisfactory for needles. Personally I dislike it as it is messy.

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The two cases of pyocyanus meningitis which occurred in a certain hospital where I worked I have already published, but there are one or two interesting points with regard to them. First, they both died and it was only after some three days had elapsed that there was any suggestion that meningitis had been present. Both patients were drowsy and complained of headache and rigidity of the neck. Both died comparatively suddenly and the course of the illness was afebrile. In the one case there was a generalized meningitis with thick pus up to the base of the brain, but pyocyanus was present in the turbid cerebrospinal fluid. In the second case the picture was complicated by the fact that the patient had a large retroperitoneal hæmorrhage which I suspect was the real cause of death.

The technique employed with these two patients was as follows. The spinal syringes were of the Record type and were kept by themselves in industrial spirit and used solely for spinal analgesia. They were rinsed with sterile normal saline together with the needles, and the skin was prepared with iodine and spirit, the anæsthetist wearing gloves. The local anæsthetic in both instances was novocain from a rubber-capped

told me that *B. coli* and *B. welchii* had been cultivated from the lumbar skin (R. A. Shabter). He thinks that it is more than probable that the lumbar skin becomes contaminated from the anus as a result of wearing pyjamas. It is also possible for organisms to be carried in by the needle, either on the point or just inside the lumen of the point. For this reason some people recommend an introducer, like the Sise introducer. On the other hand, there is the possibility of the organisms being wiped off as the needle advances in the ligamentous structures.

The literature on skin sterilization is voluminous. Personally I like old friends, and I pin my faith to soap and water first, this being followed by tincture of iodine and then spirit. My authority for this is Professor Garrod in a personal communication, and the work done by Hatfield and Lockwood whose test methods were first class and who proved to their satisfaction that iodine and spirit were highly efficient. They performed a series of experiments which were both simple and ingenious. They tested a series of skin disinfectants and were disappointed with the efficacy of the mercury preparations. They found that 95% alcohol applied to the hands for two minutes after scrubbing with soap and water proved the most effective skin preparation for the hands of personnel, but that if this was too expensive 70% alcohol was almost as effective. Alcohol, unlike CTAB, is, of course, not affected by soap.

Hatfield and Lockwood also found that for disinfection of the patient's skin 3-5% tincture of iodine, allowed to dry and followed by alcohol, which in turn is allowed to evaporate, was superior to other methods, and for this reason I remain loyal to iodine and the industrial spirit.

Although it is possible for infection to be carried in from the surface layers of the skin, I believe that meningitis, when it occurs, is introduced through the lumen of the exploring needle owing to an error in technique.

Sterilization of syringes and needles.—The report from the committee appointed by the Medical Research Council, dealing with the sterilization of syringes, recommended that syringes for spinal analgesia be all-glass and not glass and metal, for in the latter type of syringe infected clot or organisms can lodge in the interstices of the cement into which it is very difficult for the sterilizing fluid to penetrate. This committee suggests that the best method of sterilization for needles and syringes is either by dry heat at 160°C. for one hour (the thermometer being near the syringes), or by autoclaving at 120°C. for twenty minutes at 15 to 20 lb. pressure. The former of these methods is definitely inimical to the Record syringe, and the second is often so, as the temperatures are such as to melt the cement. For this type of sterilization one must therefore have glass syringes.

For years I put my syringes, taken apart, together with the needles (run through with spirit) into ordinary industrial alcohol for some ten to fifteen minutes before use. Fortunately nothing went wrong. Then I took to keeping them in industrial spirit in an airtight case. I had no cases of meningitis, and I personally have been fortunate in that I have never had a case of meningitis. The reason, I think, was due to the fact that those syringes and needles were used for nothing but spinal punctures.

I have seen syringes taken from a jar of spirit and placed ready for spinal anaesthesia. In that jar were other syringes and needles used for exploring and for aspirating pus. This practice cannot be too strongly condemned. Only the other day I saw a nurse preparing a trolley for a spinal anaesthetic. She took a syringe from a jar of spirit in which were other syringes, one of which had only been returned to the spirit some five minutes earlier. She placed the syringe in a sterile bowl and then went to the tap and ran tap-water into the bowl in order to rinse out the spirit.

The Medical Research Council Committee tells us that 90% industrial spirit will kill organisms (according to their experiments) in twenty-two minutes, and that 70 to 75% alcohol kills vegetative organisms in a much shorter time. They agree to the use of this method where the other methods are impracticable. They suggest that all-glass syringes be used and that they be immersed in 70 to 75% spirit for five minutes. The spirit must be fresh. Apparently organisms are killed by spirit but not spores; hence the emphasis on fresh spirit. (To make 70 to 75% spirit take four parts of industrial alcohol and one part of water.)

The Medical Council state that if dry heat or autoclaving is not possible, then boiling for five minutes in water is reasonably safe. I would add to that and say boil for five minutes in distilled water, for if the water in which the syringes are boiled is alkaline there is a risk of precipitating the anaesthetic as its insoluble base. Needles, too, may be boiled, and if fitted with guards they do not lose their sharp points.

The use of boiling oil for sterilization of syringes, although reminiscent of Gilbert and Sullivan, is not recommended for syringes, as the results are not uniform, although this method is quite satisfactory for needles. Personally I dislike it as it is messy.

My own preference for sterilizing all-glass syringes is boiling in distilled water in a small sterilizer, and I prefer to boil them myself and dish them up myself, picking them out of the sterilizer (which is fitted with a rising tray) with my gloved hands.

There are other possible ways in which infection may occur. I know of one case in which pyocyanus meningitis occurred, the only possible failure in technique apparently being that the trolley was not covered with a sterile mackintosh under the sterile towel. The towel became sodden with water when the syringes were dishd up and it is presumably possible that contamination arose through the towel.

The rinsing of spinal syringes with so-called sterile distilled water has caused several cases of meningitis. Wilson Smith, Professor of Bacteriology at Sheffield, examined the sterile distilled water of several hospitals. Of 223 examinations of cerebrospinal fluid and water he was able to grow water-borne non-pathogenic organisms from 89; and from sterile distilled water he could grow organisms after the bottle had been opened for a few hours. Cuthbert Dukes grew a pure culture of pyocyanus from a sample of cerebrospinal fluid sent for examination and from distilled water. The cerebrospinal fluid was otherwise normal, and the patient showed no sign of meningitis. The real culprit was discovered to be the sterile distilled water in which the syringe and needle had been rinsed before use. This water came from a winchester of sterile distilled water which had already been opened. The remedy is obvious: if you must rinse your syringe and needles in sterile distilled water, take it from a new bottle which has been freshly sterilized. Barrie (1941) was using water from a Berkefeld filter which was defective, and although the organisms grown from the water were non-pathogenic, nevertheless when they ceased rinsing their syringes in this water the outbreak of meningitis following spinal anæsthesia ceased.

I know of an outbreak of meningitis following spinal anæsthesia in which the infecting organism was *B. coli*. Pyocyanus and *Staphylococcus aureus* have been grown from the cerebrospinal fluid and from the local anæsthetic used. I have, however details of one case which occurred after spinal puncture, the infecting organism here being *Staphylococcus albus*. It is interesting to note that symptoms did not occur until nine days after the operation, when the patient complained of a slight headache and vague pains over the coccyx and sacrum on getting up. He became pyrexial next day, but there was no definite sign of disease although he was examined by a medical specialist three days later. Eventually he was lumbar punctured some four days after that, i.e. eighteen days after the operation. The fluid withdrawn was opalescent and showed a lymphocytosis. The culture proved sterile. The next day he developed meningeal signs and was lumbar punctured again, the culture again being sterile.

Two days after this the lumbar puncture produced a growth of *Staphylococcus albus* on culture. He died on the following day. By this time the cerebrospinal fluid showed polymorph cells as well as lymphocytes. Sulphadiazine proved ineffective although given intravenously in a continuous drip. At post-mortem the extradural space was filled with blood-stained purulent fluid. The subdural space contained a little thin, cloudy fluid, and the subarachnoid field had thick pale-yellow pus extending throughout the length of the cord, most marked at the lower end. The spinal cord appeared to be normal. It was interesting to note that although the dura had been punctured on three separate occasions there was only one puncture hole to be seen.

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bottle, the rubber being wiped over with iodine and the local anæsthetic withdrawn through a puncture. The spirit, syringes, the saline, and an ampoule of nupercaine from the same batch proved sterile on culture. Unfortunately the local anæsthetic bottle had been thrown away. I have no proof therefore that the local anæsthetic bottle was infected, but I strongly suspect that this was the case.

Organisms—staphylococci and *B. coli*—have been grown from so-called self-sterilizing local anæsthetic solutions on more than one occasion. However, we cannot say in the two cases I described that the novocain was actually guilty, but we cannot acquit it.

Thus, infection may occur from the anæsthetic solution—the procaine for local infiltration. The rubber-capped bottles are a real menace, though it is comparatively easy to sterilize the rubber cap by keeping it moistened with 10% chloroxylenol placed on the pad in the plastic cap, i.e. the Berry type of bottle. Alternatively, the top may be wiped over with spirit and iodine before it is pierced. Furthermore, it is possible for the novocain to become infected as a result of a previous use of the bottle.

If novocain is to be used, I prefer it from an ampoule or freshly boiled that morning. On the other hand, my resident, Maidlow, used the nupercaine itself as the local anæsthetic. In spite of the high sugar content I have never seen any ill-effects from its use into or under the skin, though I have not used it in a large series of cases.

Lastly, the use of the spinal drug itself may be the source of infection, but having seen the way the spinal drugs are prepared and the care taken in sterilization both of the ampoules and of the drug itself, the likelihood of contamination with organisms is very small indeed. For example, after sealing, the ampoules are immersed in a coloured solution under pressure so that any leaking ampoule will show at once when removed from the fluid, for its contents will no longer be colourless.

There is one possible source of infection via the ampoule, and this was brought into prominence by Hewer. Paper labels have been used on ampoules as a wartime measure because it has not been possible to get the ampoule etched as in pre-war days. Ampoules kept in spirit retain these labels, but if taken from the spirit and placed in any aqueous solution the labels float off and it is possible for organisms which have been imprisoned under the label (and therefore not killed by the spirit) to be released and thus form a source of infection. Ampoules may be kept in 70% spirit or the outsides may be sterilized by immersion in formalin vapour for twenty-four hours. To make doubly sure, never touch the ampoule with the hands but hold it in a swab.

So much then for the ways in which the infection may occur from breakdowns in technique. Are there any others? Yes, there is some evidence in favour of "chemical meningitis", but I would not overstress this. I have seen the records of five cases of light nupercaine anæsthesia which exhibited headache and vomiting, with pleocytosis in the cerebrospinal fluid. The symptoms began from one to four hours after operation and persisted for thirty-six to forty-eight hours. No organisms were grown from the cerebrospinal fluid although that counts for little according to Smith and Smith and Kremer. However, it was found that the nupercaine was slightly on the acid side, pH 5. Livingstone and others described 2 cases in a series of 4,006 nupercaine anæsthesias in which there was an increase of lymphocytes and protein in the cerebrospinal fluid accompanying mild meningitic symptoms. Culture was sterile. Barker found increased white cells twenty-four hours after spinal stavaine, and Jason and others described a lymphocytosis in the cerebrospinal fluid twelve hours after novocain in 14 out of 31 cases.

Orkin, in a summary of 45,966 cases of spinal anæsthesia by 20 different people, gives an incidence of 0.26% aseptic meningitis. Spiller and Payne reported aseptic meningitis following lumbar puncture in an epileptic. Reynolds and Wilson reported three cases following lumbar puncture in patients who had previously been diagnosed as chronic encephalitis, cerebral syphilis, and frontal tumour respectively. Livingstone and others commented on 8 cases they had collected, in which the symptoms were fever, stiff neck, positive Kernig, stupor and delirium. Cerebrospinal fluid cells (lymphocytes and polymorphonuclear leucocytes) were increased; onset of symptoms from one to sixty hours after operation. The drugs were allocaine, neocaine, nupercaine, novocain, and procaine. Of 7 cases commented on by Livingstone, Wellman, Clarke and Lambros, 4 recovered five to twenty-two days later and 3 died.

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Secondary meningitis is said to occur if a lumbar puncture is performed in bacteræmia. It was shown to be possible by Weed and others experimentally, and was confirmed by Remson. Pray's clinical experiences tend to disprove this theory.

But we are considering clean cases. My records refer to operations for hernia, interval appendicectomy, hysterectomy and so on. The infective theory is the only one which really concerns us. Although no organisms were grown from the cerebrospinal fluid in Barrie's cases, yet as soon as the water from the defective filter was stopped, there were no more cases of meningitis. Infection has been conveyed from the hands, or following multiple unsuccessful attempts at puncture, possibly from the patient's skin (*Staphylococcus albus*). Local anæsthetic has been proven to contain living organisms (*Staphylococcus aureus*, *B. coli* and ? *pyocyaneus*). Experiments were performed with a certain self-sterilizing anæsthetic solution, and it was found that staphylococci survived several hours, *B. coli* two to five hours and *B. megatherium* three days. 1:1,000 chlorocresol B.P.C. is recommended and used at Bart's for the local anæsthetic in rubber-capped bottles and appears to be satisfactory. Lastly, the sterile distilled water has proved to be anything but sterile after being once opened. We grew *B. pyocyaneus* from it at one hospital.

SPINAL PUNCTURE

May I now suggest a safe spinal technique?

The skin is prepared by washing with soap and water in the ward, followed by spirit, the back then being covered with a sterile towel. On arrival in the anæsthetic room the sterile towel is removed, and the lumbar area is painted first with iodine, which is left to dry, and then with spirit which in its turn is allowed to evaporate. The sterile towel with a hole in it is then applied.

The anæsthetist, wearing sterile rubber gloves, injects novocain, preferably from an ampoule, into the skin and then subcutaneously. All ampoules are held in sterile swabs, and a hole is made in the skin with a de Caux needle. The spinal needle is passed through this hole, and the stylet removed before the needle enters the depths of the interspinous ligament. All glass syringes and needles are boiled in distilled water.

I have stressed this question of aseptic technique as it is my opinion that when sepsis occurs in spinal analgesia it is conveyed through the lumen of the spinal needle owing to some avoidable failure in the anæsthetist's technique. See your syringes and needles boiled; then you will know that they are sterile. Boiling does not blunt needles if the points are protected. See that ampoules are kept in lysol and spirit, and even then avoid direct handling, and introduce the needle into the ampoule without touching the exterior.

I have seen syringes boiled in water which contained sodium bicarbonate, thus causing the spinal analgesic to fail. A colleague told me of something he once saw in a theatre. An anæsthetist dropped the spinal needle on to the floor, and not having another he picked it up, moved it about rapidly in the spirit for a few moments, and then completed his spinal puncture. The patient subsequently developed meningitis.

With proper technique spinal anæsthesia is safe and is the method of choice for certain operations. The risk of infection in spinal analgesia, if performed in suitable surroundings and with adequate precautionary technique, is negligible. But if there is any deviation from this, then infection can occur, sometimes with disastrous consequences.

[A short film, illustrating the points made by the lecturer, was then shown.]

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Professor L. P. Garrod supported the view that so-called aseptic or chemical meningitis was usually due in fact to bacterial infection. The presence in cerebrospinal fluid of Gram-negative bacilli derived from un-sterile water might be missed if cultures were not incubated at a temperature below 37°C. He had seen a number of such cases, due almost certainly to the contamination of lumbar puncture needles or manometers by immersion in distilled water which was supposed to be sterile, and cultivated organisms of this type

bottle, the rubber being wiped over with iodine and the local anæsthetic withdrawn through a puncture. The spirit, syringes, the saline, and an ampoule of nupercaine from the same batch proved sterile on culture. Unfortunately the local anæsthetic bottle had been thrown away. I have no proof therefore that the local anæsthetic bottle was infected, but I strongly suspect that this was the case.

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Section of Urology

President—A. WILFRID ADAMS, M.S.

[October 25, 1945]

A Consideration of Uretero-Colic Union and Some Experiences in the Operation

PRESIDENT'S ADDRESS

By A. WILFRID ADAMS, M.S.

THE EVOLUTION OF URETERO-COLIC UNION

THIS procedure is not yet standardized and some allusion to its evolution may be interesting. Surgical attention was at first mainly focused on the valvular junction of the ureters with the bladder. This was thought to have a major rôle in preventing the ascent of sepsis to the kidneys and, accordingly, Maydl in 1896 transplanted the ureteric ends "en bloc" with the trigone into the rectum. G. R. Fowler (1898) pointed out that Maydl's method was fallacious because the efficacy of the uretero-vesical valve depends on the rise of tension in a closed cavity by contents pressing constantly on its walls, a condition

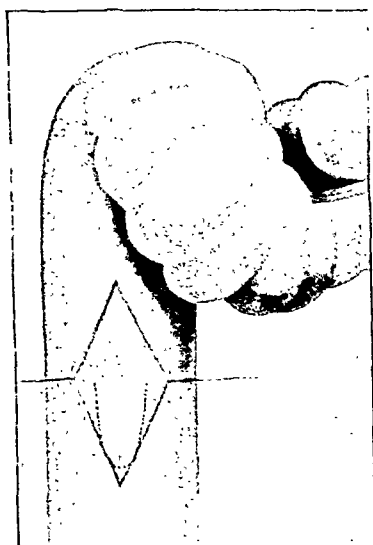


FIG. 1a.

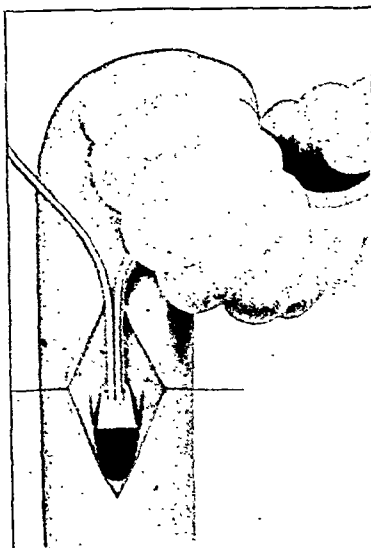


FIG. 1b.

FIG. 1.—Implantation of ureters, after Fowler, 1898 (*Amer. J. med. Sci.*, **115**, 274).

- (a) Incision on anterior wall of the rectum, including serous and muscular coats. Mucous membrane exposed in a diamond-shaped area, and the edges of the incision retracted by thread retractors. The dotted line shows line of section of mucous membrane to form the tongue-shaped flap.
- (b) Tongue-shaped flap cut, turned up, and laid upon itself (doubled back). The ureters are placed with their obliquely cut ends lying upon the surface of the flap and secured by catgut sutures in the space in the upper half of the diamond.

which prevails in the bladder but is wanting in the colon. Instead, he preferred the manoeuvre invented about the same time by Krynski (1895) who laid the ureter between the mucosal and muscular layers prior to opening into the bowel lumen and so effected a valvular insertion of the ureter. Krynski cured a man with ectopia vesicæ thus and the patient was well eight months later. Fowler sought to improve on this by adding a flap of rectal mucosa to shield the ureteric orifices (fig. 1a and b). Stress is laid on this

from the cerebrospinal fluid of most of them. Water or saline could only be safely used in this way if it came from a freshly opened bottle which had been autoclaved: the common belief that water was necessarily sterile because it was distilled was completely mistaken. The whole practice of sterilizing or attempting to sterilize surgical equipment in disinfectants and "dishing it" up in water was unsatisfactory. Sterilization by heat was the only safe method, and an alternative to boiling which was preferable in many ways was the use of dry heat. Needles and syringes could be enclosed in glass tubes and sterilized in a dry oven; they were then ready for use at any time.

Dr. R. J. V. Pulvertaft recalled a long series of cases of sepsis following spinal anaesthesia, the largest number he had seen simultaneously in one hospital was seven. In addition to meningitis, osteomyelitis of vertebrae was twice encountered.

The great features of such infections were chronicity, relapse, and multiplicity of infecting organisms; the organisms were usually of faecal type, and proteus, pyocyanus, coliform and faecal streptococci often co-existed.

Defective syringe sterilization was undoubtedly responsible for most cases; in one series in which he had been interested the syringe was shared between the theatre and a thoracic surgery ward. However, the M.R.C. instructions for syringe sterilization were not applicable to glass-metal syringes and all-glass syringes were not obtainable at present in numbers. The chief risk of syringe contamination lay in assembling wet syringes with dirty hands.

He had tested many samples of spinal anaesthetics without finding one infected; but they were not bactericidal and contained no bacteriostatic agent. There was nothing in the containers he tested to show that the samples complied with the Therapeutic Substances Act; batch numbers were not given.

He believed, personally, that spinal anaesthetics caused meningeal irritation—aseptic meningitis. He had tested the C.S.F. from a long series of cases, twenty-four hours after anaesthesia, and found excess of globulin and some increase of cells as a rule. Either all the cases were infected with some organism he could not see or grow, or the anaesthetic was irritant; and the excess of globulin provided an excellent culture medium. C.S.F. was itself a good medium. However, as he had not incubated cultures at room temperatures it was possible that certain saprophytes were present. On the other hand, these tests were done in the Middle East where "room" temperatures exceeded incubator temperatures.

Dr. R. J. Minnitt thought it might be of interest to the meeting to record that at one hospital where he worked cerebral symptoms were observed in some cases after spinal analgesia, and on investigation it was found that the powder which had been used for the rubber gloves was not sterile.

Dr. Stephen Coffin said that he considered the paper excellent, as it had dealt with many things often considered unimportant; but that he noticed that Dr. Frankis Evans' remarks had been largely in relation to hospital routine. Dr. Coffin pointed out that a sterility technique in private practice was often more difficult to attain than in hospital, as instruments had to be no less sterile yet portable and readily available; and that boiling as a means of sterilization was often not easily carried out if the only sterilizer available was occupied by the surgeon's instruments. He felt that an efficient routine for private practice needed as careful consideration as Dr. Evans had given to that for hospital, and suggested that a syringe service (such as was mentioned in para XI of Medical Research Council War Memorandum No. 15 for hospitals) could and should be organised for private practice. He said that he believed ether, lightly applied, to be the best skin sterilizer.

Squadron Leader B. G. B. Lucas said that the operation of lumbar puncture should be done under as strict an aseptic technique as any neurosurgical operation. No effort should be spared to achieve this as the consequences of sepsis inside the theca were often severe and far-reaching. The most rational way of obtaining this end was by employing as strict a "no touch" technique as possible and using a spinal introducer. All instruments were autoclaved and kept dry. The site of injection was palpated with the gloved hand through a sterile towel and marked with some antiseptic dye. Over this spot a special towel was placed with a small hole in it through which the introducer was passed.

Dr. Rex Binning said that we had been putting up with syringes of indifferent quality for too long. For sterile water he had been in the habit of using an ampoule of the water supplied with the pentothal—a practice which sometimes incurred the anger of the theatre sister but seemed otherwise free from risk.

Dr. H. W. Loftus Dale pointed out that in the film shown, the spinal needle was used for the purpose of charging the syringe with the fluid and suggested that the use of a filling needle for this purpose was preferable in so much as it eliminated the chance of contamination by contact with the outside of ampoules and labels, the danger of contamination by the glue of which had already been stressed. He also pointed out that the use of an introducing needle eliminated the risk of carrying into the subdural space the small punched-out piece of skin which may be found if the stylet does not make a dead accurate fit in the bore of the lumbar puncture needle. The use of some of the solution used for the spinal as a local anaesthetic before lumbar puncture not only enabled one to see if chance alkali contamination of the nupercaine had taken place but was a handy source of a solution of known sterility; the 20 c.c. nupercaine ampoule allowed ample for this purpose.

Dr. Frankis Evans, in reply, stated that he welcomed criticism of the film, which had been prepared rather hurriedly. Dr. Loftus Dale's comment re using the spinal needle for filling the syringe from the ampoule was pertinent. Actually, the needle used for filling the syringe was not the needle used for the spinal puncture, although the film did not make this point clear. In replying to Dr. Stephen Coffin he said that in private practice he carried a small drum containing towels, swabs, syringes, needles, &c. already autoclaved.

Section of Urology

President—A. WILFRID ADAMS, M.S.

[October 25, 1945]

A Consideration of Uretero-Colic Union and Some Experiences in the Operation

PRESIDENT'S ADDRESS

By A. WILFRID ADAMS, M.S.

THE EVOLUTION OF URETERO-COLIC UNION

THIS procedure is not yet standardized and some allusion to its evolution may be interesting. Surgical attention was at first mainly focused on the valvular junction of the ureters with the bladder. This was thought to have a major rôle in preventing the ascent of sepsis to the kidneys and, accordingly, Maydl in 1896 transplanted the ureteric ends 'en bloc' with the trigone into the rectum. G. R. Fowler (1898) pointed out that Maydl's method was fallacious because the efficacy of the uretero-vesical valve depends on the rise of tension in a closed cavity by contents pressing constantly on its walls, a condition

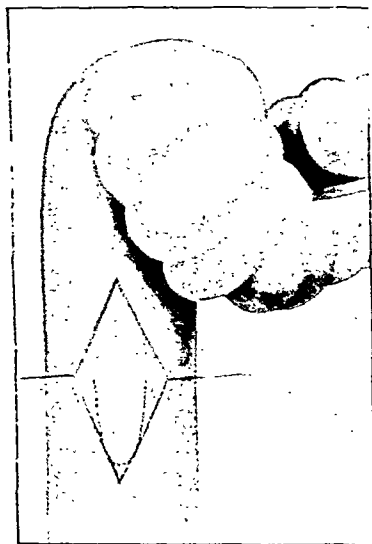


FIG. 1a.

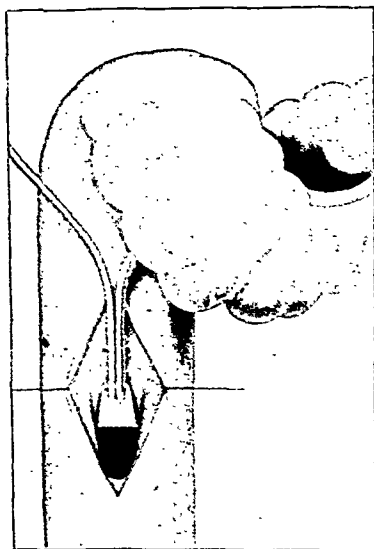


FIG. 1b.

FIG. 1.—Implantation of ureters, after Fowler, 1898 (*Amer. J. med. Sci.*, x15, 274).

- (a) Incision on anterior wall of the rectum, including serous and muscular coats. Mucous membrane exposed in a diamond-shaped area, and the edges of the incision retracted by thread retractors. The dotted line shows line of section of mucous membrane to form the tongue-shaped flap.
- (b) Tongue-shaped flap cut, turned up, and laid upon itself (doubled back). The ureters are placed with their obliquely cut ends lying upon the surface of the flap and secured by catgut sutures in the space in the upper half of the diamond.

which prevails in the bladder but is wanting in the colon. Instead, he preferred the manoeuvre invented about the same time by Krynski (1895) who laid the ureter between the mucosal and muscular layers prior to opening into the bowel lumen and so effected a valvular insertion of the ureter. Krynski cured a man with ectopia vesicæ thus and the patient was well eight months later. Fowler sought to improve on this by adding a flap of rectal mucosa to shield the ureteric orifices (fig. 1a and b). Stress is laid on this

original operation of 1896 recently by R. S. Fowler (1943), who quotes: "Placing the ureters in the submucous space of the rectal wall for a distance of three or more centimetres about the point where these enter the cavity of the rectum affords an additional safeguard against renal infection." He (G. R. F.) reported the satisfactory state of his patient a few years later; but his procedure, like that of Maydl, failed to find favour among surgeons. The fear of renal pollution still dominated the medical mind until the description by Grey Turner (1929) of a large group of successes roused the hopes and expectations of the most sceptical. He had been using Stiles' (1911) method of union after the fashion of a Witzel's gastrostomy. In the interim Coffey (1921, 1928) published his method, which virtually was a slight variant of the Krynski principle and he developed the use of an indwelling ureteric catheter. But careful analysis casts some doubt on the competence of this barrier for, presumably, in the bowel wall the ureter is only flattened out momentarily as pressure rises with peristalsis squeezing faeces past the site; whereas into its patulous mouth fluid matter of the resting bowel may pass readily. The mucosal flap over the ureteric orifices devised by Fowler as a faecal guard is ingenious, but somewhat theoretical. The situation may, nevertheless, not be as hopeless as this criticism suggests, for, still fashioning a simple union, Grey Turner (1943) reports diminishing incidence of ascending renal sepsis. Nature, too, offers further deterrents to ascending infection, viz. the regular flushing of urine in the reverse direction, as well as contraction of the ureter by its own peristalsis. Fowler (R. S.) quotes from Dr. Vaper Branch in 1912: "... that reflux is prevented much more by the ureter itself than by the obliquity of its valve". Certainly the incidence of renal infection does not appear proportional to the degree of dilatation of the ureters prior to transplantation. Sir Henry Wade (1939) advocated simultaneous bilateral transplant. He relies on the routine transfusion of isotonic sod. sulph. to prevent anuria and, by flushing the ureters, to stem the ascent of faecal sepsis.

Urinary obstruction.—Other dangers have declared themselves and engaged much surgical thought and experimentation. Not only is ascent of faecal infection to be feared but the reverse, namely, impeded down-flow of urine. This may occur early from unduly tight stitching of the bowel wall, when burying the ureter, or from subsequent oedema. Later, stenosis may ensue owing to infection and necrosis of the ureteric end with subsequent granulation and scarring. I have endeavoured to contend with these risks by following Grey Turner's lead. He warmly advocates simplicity in technique and relies on gentleness and tactful stitching, whereas others, notably Coffey and recently Wharton (1942), preserve patency by an indwelling catheter in the ureter when stitching the bowel over it. The elaborate technique of the Coffey procedure contrasts sharply with the simplicity of Grey Turner's operation. Urinary obstruction is also liable from angulation and kinking of a redundant ureter as it approaches the colon; but equally dangerous would be tension or drag of the sigmoid loop on the junction. To meet with both these contingencies I surround the colon by four stitches which tie it to the upper end of the opening of the parietal peritoneum through which the ureter is brought. Any excess ureter finds harmless accommodation retroperitoneally where, in the course of routine pyelography, surprising bends and loops are sometimes seen and compatible with satisfactory function.

Blood supply.—Some allusion is merited to the blood reaching the free end of a long length of isolated ureter. Here the evidence of Hinman and Weyrauch (1942) is valuable, that "the end often sloughs level with the rectal mucosa, though not proximal unless in instances of massive necrosis. A cross circulation from the intestine lends added vitality to the ureter soon after the first week". Operation provides a practical test and suggests that, as little blood oozes from the raw ends, the circulation is somewhat precarious in the adult. It is well to remember that Stiles was reporting operations on infants when he wrote "the ureters possess such a rich blood supply that the danger of necrosis is probably no greater with the latter (Witzel) than with the former (Maydl) procedure". A feeble circulation is helped by gentle handling aided by parietal relaxation of spinal anaesthesia, which I routinely use, the elimination of indwelling catheters that might press on delicate vessels, and tactful stitching of colon when embedding the ureters. The patient's general circulatory tone is best supported by minimum interference with normal activities. In the ordinary patient an enema on the day prior to operation assures absence of faecal accumulation. More prolonged preparation is needed in the constipated.

Earlier operation in infancy.—Thus there emerge three chief objectives in the operation—secure fusion of the tubes, a pervious passage through the ureter and its adequate blood supply. At this juncture it is appropriate to allude to what is quite unorthodox teaching by Higgins (1943) who, using the Coffey method and fusing one ureter at a time, advocates operating on cases of congenital vesical incontinence in the first year instead of waiting till the child is five. His reasons are clearly set forth and make a strong appeal. He emphasizes the high death-rate from renal infection early in the life of the unoperated

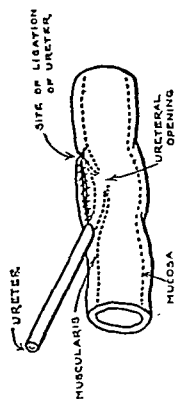


FIG. 2a.

FIG. 2 (a and b).—Experimental transplantation of the ureters, after Ferguson (Military Surgeon, 1931, 69, 184).

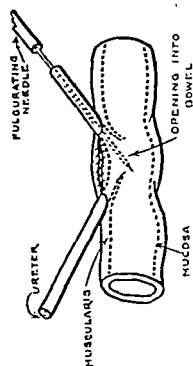


FIG. 2b.

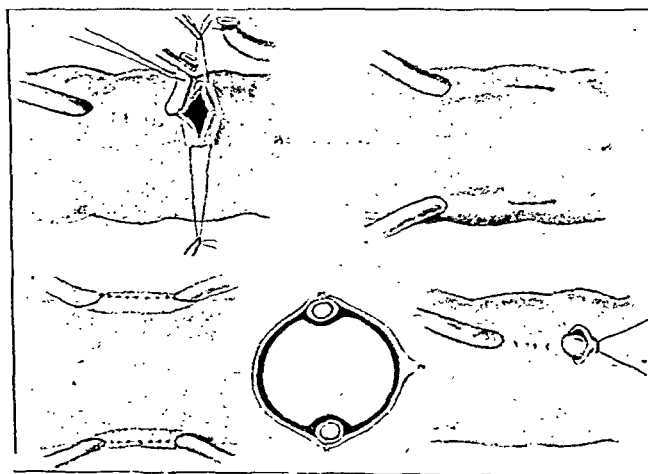


FIG. 3a.—Technique, after Winsbury-White, 1933 (*Proc. R. Soc. Med.*, 26, 1215).

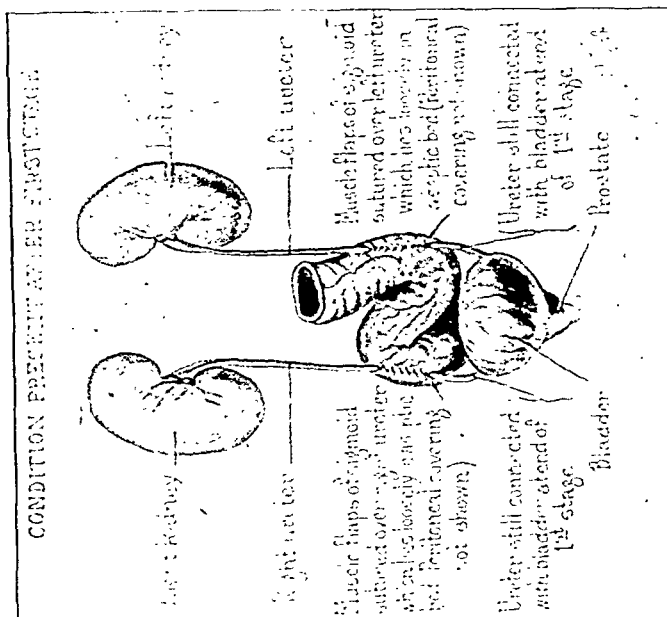


FIG. 3b.—Technique, after Jewett, 1912 (*J. Urol.*, 48, 407).

and the exclusion of this cause of failure by intervening before the wonderful potentialities of the circulation in the early months of life are lost. In support of this claim is the astonishing successful healing that follows other operations on the most puny infants in the early weeks of life, e.g. for intestinal obstruction, jaundice and, even, a $1\frac{1}{2}$ lb. nephrectomy on a child of 10 weeks (Adams, 1937), who is now a bonny girl.

Widening Field of Operation

So much for the operation to cure the life-long misery of congenital incontinence. Deviation of the urine is, however, being practised for an increasing variety of ills and even in late adult life. Of course such operations carry with them great risks. For instance, the transfer of his urine to the colonic receptacle in the sickly subject of vesical cancer is certainly a hazardous undertaking and the results of Coffey's operation, collected in 1939 by Hinman (1939), are daunting—a mortality of about 50% in 132 such cases! From their earlier brilliant successes Morson and Graham (1940) describe 13 cases of mixed pathology treated by simple technique. They report that their deaths (5) were confined to "advanced malignant disease". B. J. Ward (1936) reports a series of 7 successful cases.

Two-stage operation.—Something more seems needed, and this Ferguson (1931) may have provided by his strategic approach to the problem. He saw that while the new structure was becoming soundly consolidated there was no need to involve it in new function, any more than we tread on concrete till it is dry. He planned the operation in two stages—*form first, function second*. He fused the intact ureters to the colon while leaving the urine still flowing to the bladder. The union having thus become sealed against the access of bowel infection and assured its vitality in the new site, the ureter may then, like a bridge-graft, safely be divided at the distal end, and the lumen of the uriniferous segment be opened into that of the attached colon (fig. 2). His success in the dog was followed by that of Winsbury White (1933) in the human (fig. 3a). Substantial experimental support was added by Vermooten (1934) who, referring to the one-stage method, "showed that a conspicuous cause of failure was the immediate accessibility of the freshly opened tissue spaces within the wall of the bowel to the pathogenic bacteria in its lumen. Exudate surrounding the embedded portion of the ureter was almost inevitable. If such animals survive, the organization of this periureteral exudate will produce a mechanical ureteral obstruction, and at the same time reduce the efficiency of the uretero-intestinal valve, or destroy it entirely".

The elaboration of the two-stage fusion in the human has been most thoroughly pursued by Jewett (1942, 1943). A month after bilateral fusion of the uncatheterized ureters to the colon, he applies diathermy by a special electrode to about a centimetre of the septum separating the interiors of the blended tubes, an elaboration of the principle depicted in fig. 2. A total cystectomy is combined with this functional coalescence. Great stress is laid on the need for strict alignment of colon and ureter, conspicuous in the illustration, to exclude kinking at the junction of the tubes (fig. 3b). He reported his results in 1942 and a further series in 1944. Intestinal adhesions were his chief complication and he gives a detailed description of the most meticulous ritual to avoid their formation. Experience has proved to him that the site of fusion can be steadied adequately by a few stitches uniting the upper and lower ends of the fusion line to the parietes and, dispensing with fixation by extra-peritonization, he has saved adhesions.

Illustrations from the earlier operation of Winsbury White and Jewett's latest technique make an interesting comparison. The former is so much simpler but I have no figures of a series done in that manner. Jewett's latest results in vesical cancer are most encouraging, only one patient having died out of the last ten and that was due to pulmonary metastases. Before closing this review of the history of uretero-colic fusion, two points in Wharton's single-stage modified Coffey operation call for remark. Piercing the colonic mucosa is apt to be an awkward little manoeuvre and seems more efficiently done, as he advises, with a cautery. But his main contribution is fixation of the colonic fusion site back to the pelvic wall in such a way that the ureter lies in its natural bed. This seems the best insurance of all against strain and kinking.

Peritonitis.—This has figured less in these remarks than might seem due in view of the risks of both urinary and faecal contamination or post-operative leakage. Doubtless the adhesive type follows in some degree more or less routinely, even after the simplest procedure; but in a grossly suppurative form it is remarkable for its rarity. It is likely to figure more prominently when operating for the relief of urinary cancers or tuberculosis. At the Middlesex Hospital recently, Mr. Riches showed us *retro-peritoneal anastomosis*. He delivered the bowel, then stitched the edge of the opening in the peritoneum around the area planned for ureteric union and to this joined the proximal

ureter. This appeals as a logical means of circumventing risks to the peritoneum, though I have found smooth alignment of the two tubes more difficult. He was content to deal with one ureter only at a session, which may not halve the hazards of healing but must appreciably reduce them; and one intact ureter offers a comfortable degree of life insurance, while a transplant is "taking" on the other side.

PERSONAL EXPERIENCES

In relating my own experience of uretero-colic union it seems well to group the cases on a pathological basis. From their discussion will be gleaned indications for the operation, their differential diagnosis, points in technique, after-care and progress.

To the oldest and obvious indication for transplant—ectopia vesicæ—reference has already been made in quoting Higgins' advocacy of earlier operation. My experiences chance to be small and unprofitable to quote; but here I should like to report a much rarer congenital defect—absence of urethra—in F. P., a girl aged 5 years. She had complete incontinence and might have tempted one to resort to ureteric transplantation. Instead I tried a simple plastic closure of the bladder neck and now, two years later, she has achieved good control by day and most nights.

In regard to acquired incontinence, I have one obstetric case to report. E. S., aged 29, came, still incontinent, after four attempts elsewhere to close a vesico-vaginal fistula of two and a half years' duration. The gynæcologist still objected to uretero-colonic anastomosis, fearing kidney sepsis, so I added my plastic effort to those of my predecessors and



FIG. 4a. Pyelography before (a) and after (b), uretero-colic union for obstetric fistula.

gained a good exposure in a fat woman by a preliminary removal of pubic bones. The repair of the fistula at the bladder neck seemed promising but, despite this and ureteric catheters remaining for four days, the fistula recurred.

On 21.4.44, after pyelography (fig. 4a) and a prescribed loss of three stone in weight, bilateral uretero-colonic anastomosis was done. Total cystectomy cured the prolapsing bladder on 2.6.44. The ureters were of normal size and the method of anastomosis was that used by Grey Turner and by me in most of my cases. Although on full work and urinating three-hourly, her skiagrams now show a stone in her left kidney (fig. 4b).

Refractory Ulcerative Cystitis

While the cause of this malady remains obscure, the perpetual agony and often the ostracisms suffered by its victims are painfully obvious and led me to try relief by dysfunctionating the bladder. Included in this group with four typical female cases are a few males whose complaints were bitter enough but in whom the cystitis is of somewhat obscure pathology.

The first story is that of A. S., aged 29, married. She came in 1942 with severe dysuria and sterile slight hæmaturia. The bladder was ulcerated irregularly in a crescentic zone near the dome. As the urogram portrayed, it was a contracted and intolerant organ even with spinal anaesthesia (fig. 5a). The routine simultaneous intra-peritoneal transplant was undertaken in September 1942. Irregular fever, which is not uncommon, followed in her case. There was a suspicion of swelling in both loins and she was troubled by

and the exclusion of this cause of failure by intervening before the wonderful potentialities of the circulation in the early months of life are lost. In support of this claim is the astonishing successful healing that follows other operations on the most puny infants in the early weeks of life, e.g. for intestinal obstruction, jaundice and, even, a $1\frac{1}{2}$ lb. nephrectomy on a child of 10 weeks (Adams, 1937), who is now a bonny girl.

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natural despite its eventful history! The right uretero-colic union showed a satisfactory papilla on the bowel lumen but the left ureter ended abruptly and blindly at its junction with the serosa of the colon and had evidently undergone necrosis distal to this point. Function had been suppressed on that side where the ureter was dilated but the kidney unaffected. Obviously she had been living solely on the enlarged right kidney of which the ureter and pelvis were dilated and contained phosphatic aggregations—the source of her skiagraphic opacity—and a little muco-pus. There were merely moderate ileal adhesions to pelvic colon.

Reflection provokes the question, could this patient have been saved by early resort to uretero-colic union?

M. V., aged 24, married: She came in September 1944 with dysuria which had defied diagnosis and relief since causing her discharge from the Army a year before. Hers was a fitful history and started in childhood with urgent urination at inconvenient times. In her late teens nocturnal frequency set in and, in 1938, right renal pain. Later it came on the left and removal of that kidney was advised, but the trouble abated. She "joined up" and went to France in 1940. When urgent micturition recurred in 1943 she was put on her mettle as a case of "nerves". She tried to ignore it and took up cycling, but had to hop over the hedge too often to enjoy it! Micturition became painful and she so ill as to be mostly in bed from July to September 1943. After investigation "M & B" tablets improved her. Relapsing again in 1944 she was sent to me. I diagnosed refractory ulcerative cystitis and, as I foresaw a future of grave suffering and disability, advised diversion of the urine to the colon. The urines from both kidneys were healthy, although obvious hydro-ureter and hydronephrosis were manifest. The crescentic ragged ulceration above the ureteric orifices of a contracted bladder conformed better to refractory ulcerative cystitis than tuberculosis, and repeated search for organisms was negative. In September 1944 the routine transplantation was done of ureters dilated to the calibre of an average pencil. After the initial post-operative setback she made rapid strides and by the fourth week her urine was "clearer than before operation". She thrived well, put on weight and got her desire, joining her husband in West Africa in July 1945.

Among the males, R. P., aged 62, illustrates the efficacious result of unilateral diversion of the ureteric flow. In 1940 he came to me with a story of cystitis for ten years following catheterization for sudden retention. His frequency had become $\frac{D}{N} \frac{20}{10}$ and so agonizing that he was thrice found unconscious on the lavatory floor. The urine showed pus, *B. coli* and streptococci. There was a one-ounce hydronephrosis seen on the right and a normal left pyelogram. Cystoscopy showed a single, terraced, ovoid ulcer, about 2 cm. across, with deep necrotic base. It suggested Fenwick's solitary ulcer in the region of the right ureteric orifice. Guinea-pig tests of urine and a biopsy of the right ureter were negative for tubercle. After a preliminary cutaneous right ureterostomy and excluding cancer by palpation of the exposed thimble bladder, I turned the ureter into the ascending colon. Micturition soon became and remained normal. The intravenous pyelogram, five years later, is fair on the left but no dye is apparent on the right. In this remarkable case a bladder, the site of a refractory ulcer centring on a ureteric orifice and causing intense dysuria, was restored to normal function and the patient to full vigour by diversion of corresponding ureter to colon with consequent defunctionation of that uretero-vesical junction.

F. P., aged 57, is another case of inveterate, intensely painful cystitis but in which transplantation came too late. About the right third of his bladder showed leukoplakia, having a uniform icing-sugar appearance of sharp rounded outline when I first cystoscoped him in 1943. His past history included removal of testicle, which proved to be tuberculous in 1924, and since then pain in the right loin. In 1934 vesical instillation of calomel oil had eased cystitic symptoms till, in 1943, after right renal colic, he passed a small stone and since then pain had recurred. Nothing but a few *B. coli* were found in his urine. Lupus of bladder was considered but guinea-pig inoculation proved negative as did biopsy of the scarred right kidney which I found on exploration. I failed to catheterize the right ureter. Urine from the left was healthy. Pyelograms were fairly dense. By January 1945 there was added to the spectacular leukoplakia, general engorgement and ragged ulceration. Left extra-peritoneal transplant was done as a desperate measure but he died ten days later. The sketch of the specimen (Fig. 6) shows the very interesting ascent of the leukoplakia two inches up the right ureter where, as on the bladder mucosa, its outline was sharply demarcated. That kidney was grossly septic. The left kidney and ureter appeared clean, except at the anastomotic level where the lining was sloughing and a small abscess in the uretero-colic interval exuded pus into the ureter. It appeared well walled-off.

The final revelation rouses speculation regarding aetiology. Was not infection, possibly tuberculous, of the right kidney responsible for this obscure vesical lesion and the latter curable in its early history by nephrectomy; or, in the later stage, would not defunctionation of the bladder be the only hope?

W. W., aged 63, came with an intolerable cystitis of some five years' duration and I diagnosed a primary refractory ulcerative cystitis. The only way out of his misery appeared to be by the drastic remedy of defunctionating the bladder. I performed left uretero-colic union on 30.5.45, and was delighted with the prompt benefit. But his old symptoms are back again and diarrhoea in addition. I am deterred from completing the diversion of urine from the bladder with right ureteric transplant, which would seem the logical procedure, owing to a startling radiographic discovery—gross calcification in his prostate! This invalidates my original opinion, will probably alter the treatment and teaches the grave responsibility of infallible diagnosis before embarking on a profound and irrevocable transgression on the body.

another frequent post-operative discomfort—that of flatulent distension. This may be relieved by the regular passage of a flatus tube every four hours, which also prevents the accumulation of urine in the bowel during the first few days. When she visited the ward again three months later her much improved aspect disguised her identity from the ward Sister. Despite her clinical well-being, radiography, 10.3.43 (fig. 5b), reveals obvious dilatation of ureters and kidneys. The current picture is the same. She remains delighted, at full work and urination is usually only five-hourly and not at night but, with a cold, may be every two hours.

She recently asked: "May I have a child?" Her blood urea is 0.060% and her weight does not increase so I shall warn her of the risk. Many will recall Grey Turner's triumphant picture of a woman with the four children she bore after ureteric transplant.

Since the above was written she has died from a brief attack of uræmia, December 1945. Yet the post-mortem showed a reconstructed urinary system which was apparently satisfactory.

D. G. came first in 1937 at the age of 21. Repeated diathermy to a patch of ulceration in the fundus was ineffectual so, in 1938, I operated. Cystotomy cut the ulcer in twain. It was a discoid lesion, about two centimetres in diameter, raised like a button in the bladder wall the whole thickness of which was excised. The removal appeared complete and the pathologist reported "appearances agree with Hunner's elusive ulcer of the bladder". She resumed full work, looked radiantly healthy and lost her pain and frequency but, contrary to my advice, married in October 1939. Her symptoms at once returned and she became a social outcast. Cystoscopy confirmed the cystitis and healthy urines in the ureteric specimens. Pyelograms in 1937 had been normal but by 1943 showed marked hydro-ureters and renal dilatation. Pain in her loins and, finally, hæmaturia reconciled her to uretero-colic union in February 1943. Faced with mega-ureters I offered her a transplantation of one ureter at a time, but she would only consent to a single intervention. At this operation a technical difficulty declared itself in the

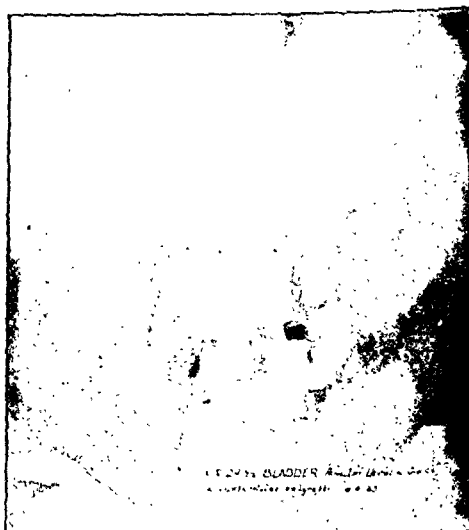
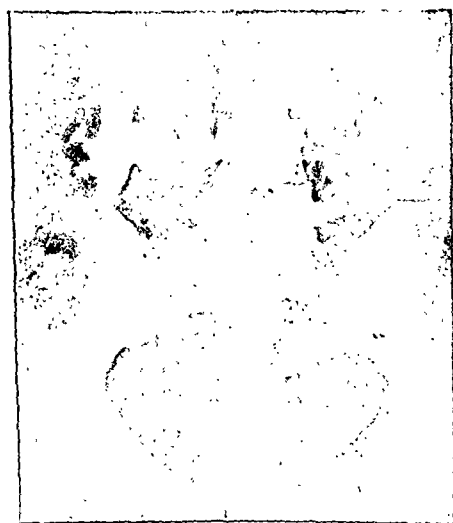


FIG. 5a.

FIG. 5b.

FIG. 5 (a and b).—A. S. Pyelography before (a) and after (b), uretero-colic union for refractory ulcerative cystitis.

tendency of a large ureter and the necessary enfolding of the colonic wall to encroach obstructively on the bowel lumen. Her convalescence was an anxious time with recurrent fever, headache, vomiting and pain and foul discharge on lavage of bladder. Urination was satisfactory and only once was tenderness in the right loin present.

The reward for effort came a year later when her husband wrote: "Everyone still cannot believe that my wife is enjoying such good health after suffering so long." In June 1945 urination was three to six times by day and once at night. She had done an ordinary wartime job for a year and was adopting an infant.

F. W., aged 44, told a like story of long, painful and incapacitating illness. Cystitis had already troubled her for two years when first I saw her in 1939, frail in form and voice and with a pale waxen countenance. Irregular ulcerous areas at the back of the bladder increased despite diathermy. It was in her case that one of the excavations was seen oozing blood during cystoscopy and the bladder ruptured into the peritoneum. She survived immediate laparotomy and, indeed, the result was surprising amelioration of symptoms but, later, she deteriorated and consented to the desperate uretero-colic union. This was preceded by pyelography, and precautionary sigmoidoscopy, as diarrhoea also had become a serious worry. The operation was on 9.8.44, and convalescence anxious, but she was gratified with her new "water-works" till terminal pyelonephritis developed this spring and urography showed a calculous cast of the right pelvis. She died on 9.6.45. Post-mortem showed the bladder lining smooth and shiny but the organ otherwise notably

natural despite its eventful history! The right uretero-colic union showed a satisfactory papilla on the bowel lumen but the left ureter ended abruptly and blindly at its junction with the serosa of the colon and had evidently undergone necrosis distal to this point. Function had been suppressed on that side where the ureter was dilated but the kidney unaffected. Obviously she had been living solely on the enlarged right kidney of which the ureter and pelvis were dilated and contained phosphatic aggregations—the source of her skiagraphic opacity—and a little muco-pus. There were merely moderate ileal adhesions to pelvic colon.

Reflection provokes the question, could this patient have been saved by early resort to uretero-colic union?

M. V., aged 24, married. She came in September 1944 with dysuria which had defied diagnosis and relief since causing her discharge from the Army a year before. Hers was a fitful history and started in childhood with urgent urination at inconvenient times. In her late teens nocturnal frequency set in and, in 1938, right renal pain. Later it came on the left and removal of that kidney was advised, but the trouble abated. She "joined up" and went to France in 1940. When urgent micturition recurred in 1943 she was put on her mettle as a case of "nerves". She tried to ignore it and took up cycling, but had to hop over the hedge too often to enjoy it! Micturition became painful and she so ill as to be mostly in bed from July to September 1943. After investigation "M & B" tablets improved her. Relapsing again in 1944 she was sent to me. I diagnosed refractory ulcerative cystitis and, as I foresaw a future of grave suffering and disability, advised diversion of the urine to the colon. The urines from both kidneys were healthy, although obvious hydro-ureter and hydronephrosis were manifest. The crescentic ragged ulceration above the ureteric orifices of a contracted bladder conformed better to refractory ulcerative cystitis than tuberculosis, and repeated search for organisms was negative. In September 1944 the routine transplantation was done of ureters dilated to the calibre of an average pencil. After the initial post-operative setback she made rapid strides and by the fourth week her urine was "clearer than before operation". She thrived well, put on weight and got her desire, joining her husband in West Africa in July 1945.

Among the males, R. P., aged 62, illustrates the efficacious result of unilateral diversion of the ureteric flow. In 1940 he came to me with a story of cystitis for ten years following catheterization for sudden retention. His frequency had become $\frac{D}{N} \frac{20}{10}$ and so agonizing

that he was thrice found unconscious on the lavatory floor. The urine showed pus, *B. coli* and streptococci. There was a one-ounce hydronephrosis seen on the right and a normal left pyelogram. Cystoscopy showed a single, terraced, ovoid ulcer, about 2 cm. across, with deep necrotic base. It suggested Fenwick's solitary ulcer in the region of the right ureteric orifice. Guinea-pig tests of urine and a biopsy of the right ureter were negative for tubercle. After a preliminary cutaneous right ureterostomy and excluding cancer by palpation of the exposed thimble bladder, I turned the ureter into the ascending colon. Micturition soon became and remained normal. The intravenous pyelogram, five years later, is fair on the left but no dye is apparent on the right. In this remarkable case a bladder, the site of a refractory ulcer centring on a ureteric orifice and causing intense dysuria, was restored to normal function and the patient to full vigour by diversion of corresponding ureter to colon with consequent defunctionation of that uretero-vesical junction.

F. P., aged 57, is another case of inveterate, intensely painful cystitis but in which transplantation came too late. About the right third of his bladder showed leukoplakia, having a uniform icing-sugar appearance of sharp rounded outline when I first cystoscoped him in 1943. His past history included removal of testicle, which proved to be tuberculous in 1924, and since then pain in the right loin. In 1934 vesical instillation of calomel oil had eased cystitic symptoms till, in 1943, after right renal colic, he passed a small stone and since then pain had recurred. Nothing but a few *B. coli* were found in his urine. Lupus of bladder was considered but guinea-pig inoculation proved negative as did biopsy of the scarred right kidney which I found on exploration. I failed to catheterize the right ureter. Urine from the left was healthy. Pyelograms were fairly dense. By January 1945 there was added to the spectacular leukoplakia, general engorgement and ragged ulceration. Left extra-peritoneal transplant was done as a desperate measure but he died ten days later. The sketch of the specimen (Fig. 6) shows the very interesting ascent of the leukoplakia two inches up the right ureter where, as on the bladder mucosa, its outline was sharply demarcated. That kidney was grossly septic. The left kidney and ureter appeared clean, except at the anastomotic level where the lining was sloughing and a small abscess in the uretero-colic interval exuded pus into the ureter. It appeared well walled-off.

The final revelation rouses speculation regarding aetiology. Was not infection, possibly tuberculous, of the right kidney responsible for this obscure vesical lesion and the latter curable in its early history by nephrectomy; or, in the later stage, would not defunctionation of the bladder be the only hope?

W. W., aged 63, came with an intolerable cystitis of some five years' duration and I diagnosed a primary refractory ulcerative cystitis. The only way out of his misery appeared to be by the drastic remedy of defunctionating the bladder. I performed left uretero-colic union on 30.5.45, and was delighted with the prompt benefit. But his old symptoms are back again and diarrhoea in addition. I am deterred from completing the diversion of urine from the bladder with right ureteric transplant, which would seem the logical procedure, owing to a startling radiographic discovery—gross calcification in his prostate! This invalidates my original opinion, will probably alter the treatment and teaches the grave responsibility of infallible diagnosis before embarking on a profound and irrevocable transgression on the body.

FIG. 7.—F. L. Section of cancerous bladder and internal genitals removed after uretero-colic union.

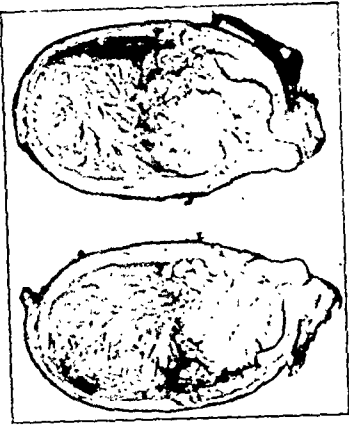
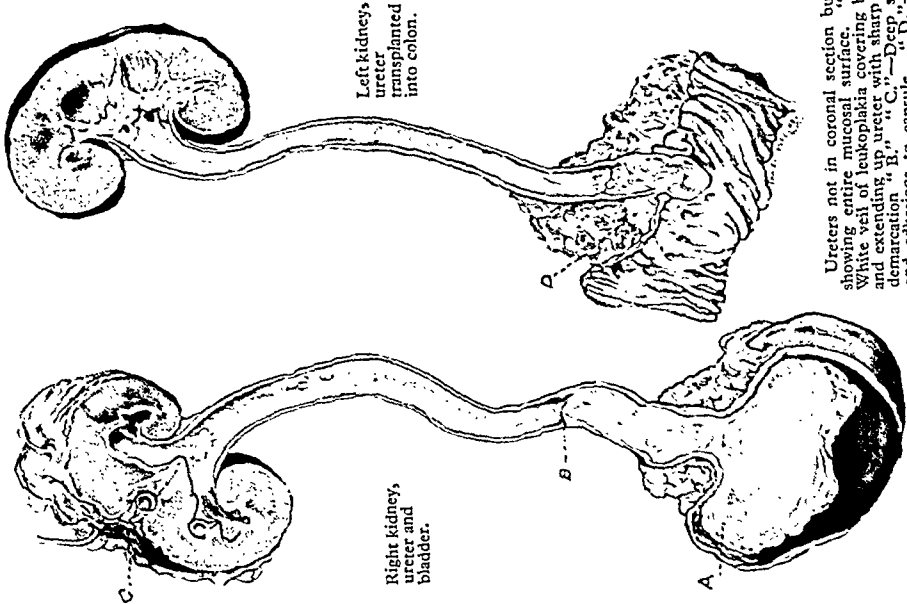


FIG. 8.—Post-mortem specimen four months after creation of new urinary tract—excised bladder. In section shows union between kidneys.



Left kidney's ureter transplanted into colon.

Right kidney, ureter and bladder.

Ureters not in coronal section but split showing entire mucosal surface. "A."—White veil of leukoplakia covering bladder and extending up ureter with sharp line of demarcation "B." "C."—Deep scarring and adhesions to capsule. "D."—Small abscess at colo-ureteric interval extruding pus into ureter (F. T., 5, 57 years).

FIG. 6.—F. P. Post-mortem specimen after uretero-colic union for inveterate leukoplakia of bladder and right ureter.

Tuberculous Cystitis

Specific infection of the bladder may also cause intense incurable suffering and I have been glad to try ureteric transplant to ease the sad lot of two tuberculous cases.

R. W., aged 10 years, is a boy whose painful frequency of many months, with urine repeatedly sterile, I attributed to vesical calculi. His complaint did not abate after litholapaxy and further investigation led me to suspect the right kidney as the "fons et origo" of his trouble. (Pyelography 7.12.43.) Accordingly, on 11.1.44, I explored the loin and removed a tuberculous kidney and ureter. The large kidney was a shell expanded by tuberculous pus and calcareous material, which provided the obvious source of the vesical pathology. Healing was quick and he was discharged to a sanatorium. However, by May 1944, micturition had become so excruciating that his heartrending cries led neighbours to protest. On readmission the house surgeon tried to free debris blocking the urethra, but it was obvious the child was nearing his end so the parents allowed me to turn the flow of urine from the residual left kidney into the colon. Reaction was alarming and, despite intravenous fluids, urine did not appear from the bowel for five days. On 15.6.44, four ounces of pus were drained from the dorsum ili and formal cystostomy done after finding copious foul discharge expressible *per urethram*. Cystitic pain and discharge compelled me to complete the procession of operations by total cystectomy and vesiculo-prostatectomy on 6.7.44. He soon healed, learnt to use his bowel conveniently and became quite a cheery little fellow. A tendency to flat foot has been cured by cycling, but he puts on little weight and now has a blood urea of 95 mg.%. If we cannot hope to give him length of life, at least he is proceeding happily whilst it endures. How much mutilation, suffering and major surgery might have been saved by timely diagnosis!

In the second case, B. L., aged 27, the primary left renal source of her urinary tuberculosis had been removed two and a half years before she reached me in July 1945. She was still disabled and pale with moderate frequency, pain in the right loin and a blood urea of 100 mg.%. Transplant of the right ureter to bowel seemed the only hope for her future. Cystoscopy confirmed the presence of tuberculous ulceration and this was the cause of a dilated right kidney and ureter. Urine from the latter was guinea-pig positive.

These are early days but they are her first delightful ones for a long time and her weight is obviously increasing. "Is there any preferable alternative?" appears a legitimate question.

Vesical Carcinoma

Just as vesical defunctionation has brightened the dark corners of cystitic pathology, so it is offering great promise in the gloomy sphere of bladder cancer. This disease, while unfavourable for conservative surgery, is relatively slow to spread from the bladder. If, therefore, we can treat it radically and dispense with the bladder, the patient's prospects of effective succour are good.

My experience is but recent and starts with a man, F. L., aged 36, sent to me on 30.3.42 with pain and intermittent hæmaturia. Diathermy was tried tentatively but, six months later, a radical operation became imperative and a hydronephrosis had enlarged the right kidney four times. On 2.10.42 I transplanted a normal left ureter to the colon and performed a right cutaneous ureterostomy with corresponding nephrectomy a month later. On palpation of the bladder the growth was felt the size of an orange but movable. Two months after the transplantation, total cysto-prostatectomy was performed, as usual under spinal anaesthesia (fig. 7). Occasional gas and oxygen is added in a few cases. The peritoneal veil remained inviolate. After an eventful convalescence he resumed light work the following summer and, this October (1945), tells me he has only been off work five days in the past two years. Urination is $\frac{D\ 6-8}{N\ 1}$; he

is cheerful, the abdomen feels healthy and he maintains his weight at 11 stone. His blood urea figure is 0.038%, but the pyelogram is of subnormal density and mildly dilated.

G. P., aged 42, came first to me on 29.1.43, having a sixteen months' history of increasing painful frequency and hæmaturia which had already been treated by diathermy and cystostomy. The lesion was obviously advanced carcinoma showing a filling defect with crenated outline in the cystogram and bilateral hydronephrosis. At the transplantation I noted the bladder was the size of a lemon and no extension of the disease beyond it. Swabs of ureteric urines proved to be sterile. The post-operative pyelograms showed full function on the left side and about 50% on the right, which is significant as distension of the right ureter had been noted at the operation. After total cysto-prostatectomy, on 12.5.43, he got on fairly for two or three days but died of obstruction on the fifth day. Post-mortem showed the new urinary drainage system in good working order. There was moderate pelvic peritonitis but the lethal factor was a band acutely obstructing the last two feet of the ileum. A broad adhesion joined the terminal ileum to the pelvic colon. These were due to peritonitis around the previous anastomosis. The newly created effluent system, right ureter included, looks competent in the photo of the specimen and the cadaver appeared clear of neoplastic remains (fig. 8). How poignant are the surgeon's regrets over the fatal adhesions incidental to uretero-colic union, and how pregnant the precautions advocated by Jewett for minimizing such!

H. M., aged 40, started in April 1944 a dull ache in front and back of sacro-iliac region. Frequent painful micturition was gradually added and, by August, blood in the urine which recurred till he came to me in November. He looked in fair health

but obviously distressed. A malignant papilliferous tumour was found on cystoscopy, encircling the bladder neck. The ureters were joined to the colon on 14.11.44, and hiccoughs were notable in an otherwise smooth healing. Six weeks later he had total vesico-vesiculo-prostatectomy and went home well on the eighteenth day. Reviewed on 8.10.45, he looks and feels well. Urination is $\frac{D\ 6-8}{N\ 1-2}$ blood urea was 36 mg.% and post-operative pyelograms show healthy structure. His only complaint is weakness in the back with heavy work.

W. H. J., aged 54, is still more recent, coming in January 1945 with malignant tumour choking the outlet of his bladder which was half-way up to the navel. Hæmaturia troubled him for the previous nine months and marked frequency had supervened. For this man of light build and rather waxy hue the sole effective remedy involved ureteric transplantation which was done on 9.3.45, and he went home in the third week. Bladder washes were done and acute epididymitis allowed to settle, prior to the total cystectomy, 4.5.45. Dr. A. D. Fraser reports: "This is a carcinoma . . . composed of rapid and irregularly growing cells of Malpighian cell layer type . . . marked infiltration of the bladder wall." He is (16.10.45) quite cheerful and wants to start work. He still wears a spare aspect and has recently felt pain in the left groin for which no physical signs are forthcoming apart from a few tender shotty glands. His frequency is $\frac{D\ 3-4\ \text{hourly}}{N\ 3-4\ \text{times}}$ and pyelography shows the left kidney twice its normal size and the right one and a half times.

E. W., aged 69, came in January 1943 the victim of advanced vesical cancer and super-added cystitis. She was the victim, too, of Mars for, having resorted to her doctor two years previously and been labelled cystitis, she was blitzed to a hospital in another town and, when she returned, found her doctor gone to the war! Her incessant vesical spasms were ghastly to behold and I performed ureteric transplantation. She succumbed three days later and autopsy showed a clean peritoneum and clean right ureter but the left was clogged with blood down to a short indwelling tiny rubber tube, the only one used in this series. Kidneys and bladder were grossly septic. Four cancerous foci were seen on base, back and dome of bladder but no extra-vesical deposit.

My last case, Q. P., aged 35—almost equally harrowing a sight and destitute of hope—started her illness in May 1944 with soreness just within the vagina which became severe by September. By January 1945 suprapubic cystostomy was done owing to super-added dysuria and radium used shortly after for urethral cancer. The urogram, when she came to me in August, was informative, revealing good renal excretion. A large hard mass of growth behind the pubes was felt ineradicable, but diversion of urine to the colon offered a faint hope of alleviating her ghastly lot. She died twelve days after the operation and, probably, of terminal collapse of lower lobes of her lungs. The transplants had taken satisfactorily but pyonephrosis and several tiny abscesses had affected the right kidney and in the left was recent mild pyelonephritis. The primary involved the urethra and bladder base and was fused to the symphysis pubis and associated with a few hepatic nodules suggestive of secondary spread. Presumably it started in the urethra.

While the operation earlier might have paved the way to surgical cure of the cancers it was only used as a desperate last resort in these two women. It failed, but nevertheless I believe it worthy of trial as a palliative in some cases of this most distressing form of cancer.

Disease	Total	Op. mort.
Obstetric fistula	1	—
Refract. ulc. cystitis: M.3*, F.4	7	1
Tuberculous cystitis: M.1†, F.1	2	—
Carcinoma vesicæ: M.4, F.2	6	2
	16 (11 bilateral)	3 (2 bilateral)

*Precise pathology uncertain.

†Boy of 10 years—all others adults.

The three fatal cases were so ill prior to operation as to need no further comment. Apart from the obstetric category, the material handled obviously involves a high operative risk so that the results are far from discouraging.

Two cases have died subsequently. One (F. W.), with pyelonephritis, had been a very sickly female for years and the operation played but a small part in her ending. The other (G. P.), with acute obstruction, ranks as a serious surgical disaster pointing to the dangerous complication of adhesive peritonitis.

The Latent Morbidity

What moves me more than the mortality is the *insidious morbidity*, masked clinically by the patients dominating sense of well-being, that often follows this operation. Most cases show dilated urograms and one patient a stone in the kidney. Their weight is apt to be stationary and the blood urea raised. In fact, these features point to early renal impairment; and it is this, rather than infection, that seems to me still to leave the future of these patients somewhat clouded. Is not inflammatory reaction in the colonic bed of the ureter, resulting in fibroses, the pathological crux of the undertaking? To minimize this peri-ureteritis and urinary stasis, the procedure demands most meticulous surgical

performance and, in the seriously-ill types, I hope to try the extra insurance afforded by the two-stage principle introduced by Ferguson and admirably developed by Jewett with his highly specialized technique.

CONCLUSION

From the foregoing it is clear that the operation has established a permanent and important niche in the surgery of many serious vesical disorders. In a minority, it is well that a few weeks should elapse between the transfer of right and left ureters. In a still smaller group, the diversion of one ureter alone may be curative—the patient may have but one. But, whether in certain cases the retro-peritoneal junction represents a real advance, time must decide.

I herewith acknowledge my great collective debt to authors and publishers for their permission to borrow both text and illustrations, and to workers whose names do not appear in the bibliography.

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[November 29, 1945]

True Aneurysm of Left Renal Artery.—A. J. HERIOT, F.R.C.S.

Mrs. S., aged 49. First seen on 4.12.44. Her complaints were of a swelling in the left side of the abdomen, first noticed five months previously and which had increased in size and, further, there was now a throbbing sensation. She was known to have suffered from high blood-pressure for the previous three years.

Past history.—Nothing significant. Has two children, aged 21 and 22. No history of injury.

Clinical examination revealed that there were two parts to the swelling in the left abdomen—one in the loin, which was definitely renal, without pulsation or bruit—whilst internal to that there was a pulsating tumour, almost certainly aneurysmal. The appearance of the pyelography and retrograde films suggested that this tumour arose from the renal artery rather than from the aorta or splenic vessel.

The following tests were carried out:

Urea concentration test:	Time	Volume	Urea%
	1st hour	40 c.c.	2.3
	2nd hour	62 c.c.	2.65
	3rd hour	37 c.c.	2.4

Blood urea 37 mg. %

Wassermann reaction negative.

Urine: An occasional red blood corpuscle and granular cast seen—otherwise normal.

The blood pressure on admission was 235/145 but with rest in bed prior to operation, the lowest figure was 175/95.

It was felt justifiable to explore this tumour and this was carried out on 15.12.44 by an anterior approach, employing a T incision. Operation confirmed a large aneurysm of the renal artery which, with some difficulty, was freed from the aorta and a short pedicle ligated. Specimen showed a very large aneurysm of the renal artery compressing and deforming the pelvis and histological examination revealed an extreme degree of renal ischaemia. The report on the specimen was as follows: "Compression of the kidney has led to destruction of the normal histological appearances with extensive tubular atrophy. Marked pathological changes are present in the glomeruli and their afferent arterioles. All degrees of hyaline change can be seen in the former, from peri-glomerular fibrosis and early hyalinization with shrinkage of the tuft to, in the majority of cases, complete obliteration

of the glomerulus. No normal glomeruli were seen. Similar severe hyaline changes were seen in the arterioles, which in many cases were completely obstructed. Collections of lymphocytes and a collection of acute inflammatory cells, polymorphs and eosinophils, were present in the kidney and perirenal tissue, and there was also a diffuse scanty infiltration of polymorphs. There was evidence of recent hæmorrhage, probably operative in origin. The general histological picture suggests that an extreme degree of renal ischæmia was present. The wall of the aneurysm consists of rather œdematous fibrous tissue, some of which shows hyaline changes. No endothelial lining was seen. Collections of lymphocytes were present in the wall, many of them containing reticulum cells and having the appearance of true germinal follicles. In some cases these lymphocytic collections were situated in the neighbourhood of the vessels. There was also a little patchy plasma cell infiltration.

Following operation her blood-pressure fell to 130/80 but on final discharge on 27.2.45 it had reached 165/105, whilst examination on 24.11.45 showed a reading of 205/120.

Commentary.—The interesting features of this case are the extreme rarity of renal aneurysms, especially of such a large size, and in this case there is no apparent ætiological factor, although in most previous cases, trauma would appear to be the cause. This kidney, too, exhibits the phenomenon of a Goldblatt kidney, but, despite nephrectomy, after a year the blood-pressure has risen to almost its previous height although the initial fall had been encouraging.

I am very grateful to Mr. J. B. Hunter for permission to treat this case and to Mr. Yates Bell for his help and advice.

Double Urethra in a Male.—J. D. FERCUSSON, F.R.C.S.

True duplication of the male urethra, whether in conjunction with a single or double penis, is a rare anomaly. Slightly less uncommon are those accessory channels which, by reason of their length, are clearly distinguishable from the small blind pits encountered on the glans penis, and around which controversy has raged as to whether they should be regarded as urethral homologues. The case here described belongs to the latter type and exhibits features of interest with regard to its morphology.

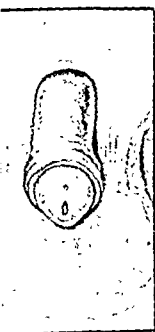


FIG. 1.

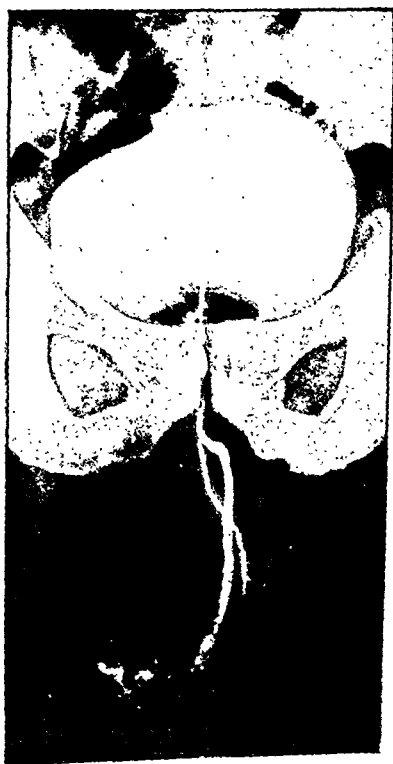


FIG. 2.



FIG. 3.

L. B., a male patient aged 32, was admitted to the Central Middlesex County Hospital on account of a right-sided epididymo-orchitis of a non-specific nature. On routine examination he was found to possess, in addition to a normally placed urethral orifice, a second smaller aperture opening on the dorsum of the glans (fig. 1). Although no discharge was evident from the normal urethra, the abnormal dorsal orifice emitted a thin white sticky fluid. No specific organisms were detected in this discharge, which had been present for a few days, and there was no history of venereal infection. He stated that he micturated solely through the normally placed aperture, but, that when ejaculation of semen occurred (also from this opening) there was a thin watery discharge from the abnormal channel.

Following the subsidence of the epididymo-orchitis and diminution of the discharge, it was found possible to pass a probe through the small dorsal opening into a sub-cutaneous channel running for a distance of 14 cm. in the dorsal mid-line of the penis. This channel passed beneath the symphysis pubis and seemed to terminate in the prostatic region. Injection of radio-opaque fluid through a ureteric catheter passed into the channel, showed a serpentine continuation at this point, suggestive of a connexion with the right seminal vesicle. Simultaneous urethrocystography was performed through the normally placed urethra, and the combined appearance is shown in the accompanying photograph and diagram (figs. 2 and 3).

From these it will be seen that the normal urethra communicates with the bladder in the usual manner, while the abnormal channel is apparently quite distinct and ends as described above.

The main points of interest in this case appear to be:

(1) The co-existence of right epididymo-orchitis and a discharge only from the dorsally placed aperture, examined in the light of the urethrographic findings.

(2) The anatomical relationship between such dorsally placed channels and the position of the urethra in cases of penile epispadias with sphincteric control.

Owing to the possibility of predisposing the left side of the genital tract to infection, posterior urethroscopy, with a view to establishing the position of the ejaculatory ducts by catheterization, has not been proceeded with.

A somewhat similar case, in which an abnormal dorsal channel communicated, by divarication around the prostate, with both seminal vesicles is recorded by Cruveilhier (1852). A detailed account of further accessory channels is given by Lebrun (1912), and Mackenzie (1916). It is of interest to note that such duplicated "urethras" frequently emit a discharge, the persistence of which may, in some cases, call for extirpation of the track.

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Spinal Anæsthesia and its Effect on a Case of Hydronephrosis and Hydro-ureter.—

Squadron Leader HUGO GRANT, R.A.F.

The treatment of achalasia of the intestine by spinal anæsthesia was first shown to be a possibility by Stabins, Morton and Scott when they found that certain cases of megacolon, in which spinal anæsthesia had been used to gauge the effect of a proposed subsequent sympathectomy, were so much improved following the spinal anæsthesia that the sympathectomy was not required. Telford and Simmons reported 7 cases treated and also 1 case of achalasia of the œsophagus also treated with excellent results. A further case of achalasia of the colon was also reported by Court and Hasler.

Ogier Ward treated a case of bilateral hydro-ureter by pre-sacral neurectomy with excellent results—the contraction persisted eleven months later.

The autonomic nerve supply to the urinary tract is as follows:—

The sympathetic innervation is from the renal, testicular and hypogastric plexuses, and supplies the whole of the urinary tract from kidney to the bladder.

The para-sympathetic through the vagus supplies the kidney parenchyma, and through the sacral para-sympathetic supplies the bladder.

As far as is known there is no para-sympathetic supply to the pelvis or ureter.

An analogy between achalasia of the urinary tract and achalasia of the intestine may be observed in that the obstruction of megacolon is said to be related to the fact that this disorder occurs where the sacral para-sympathetic takes over from the vagus.

of the glomerulus. No normal glomeruli were seen. Similar severe hyaline changes were seen in the arterioles, which in many cases were completely obstructed. Collections of lymphocytes and a collection of acute inflammatory cells, polymorphs and eosinophils, were present in the kidney and perirenal tissue, and there was also a diffuse scanty infiltration of polymorphs. There was evidence of recent hæmorrhage, probably operative in origin. The general histological picture suggests that an extreme degree of renal ischemia was present. The wall of the aneurysm consists of rather œdematous fibrous tissue, some of which shows hyaline changes. No endothelial lining was seen. Collections of lymphocytes were present in the wall, many of them containing reticulum cells and having the appearance of true germinal follicles. In some cases these lymphocytic collections were situated in the neighbourhood of the vessels. There was also a little patchy plasma cell infiltration.

Following operation her blood-pressure fell to 130/80 but on final discharge on 27.2.45 it had reached 165/105, whilst examination on 24.11.45 showed a reading of 205/120.

Commentary.—The interesting features of this case are the extreme rarity of renal aneurysms, especially of such a large size, and in this case there is no apparent ætiological factor, although in most previous cases, trauma would appear to be the cause. This kidney, too, exhibits the phenomenon of a Goldblatt kidney, but, despite nephrectomy, after a year the blood-pressure has risen to almost its previous height although the initial fall had been encouraging.

I am very grateful to Mr. J. B. Hunter for permission to treat this case and to Mr. Yates Bell for his help and advice.

Double Urethra in a Male.—J. D. FERGUSON, F.R.C.S.

True duplication of the male urethra, whether in conjunction with a single or double penis, is a rare anomaly. Slightly less uncommon are those accessory channels which, by reason of their length, are clearly distinguishable from the small blind pits encountered on the glans penis, and around which controversy has raged as to whether they should be regarded as urethral homologues. The case here described belongs to the latter type and exhibits features of interest with regard to its morphology.

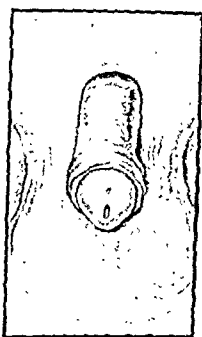


FIG. 1.

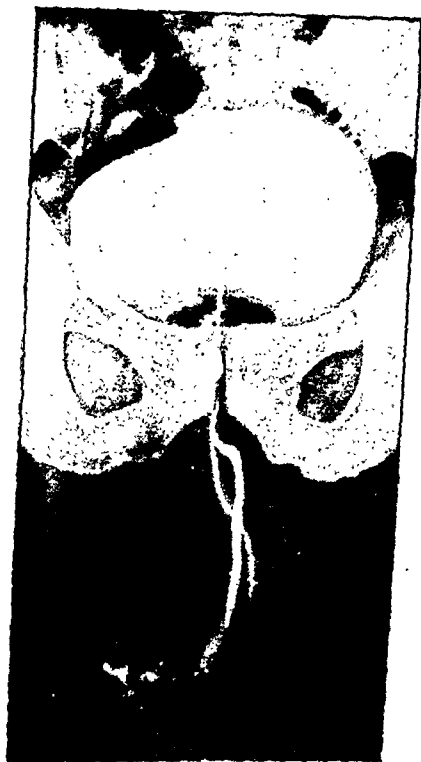


FIG. 2.

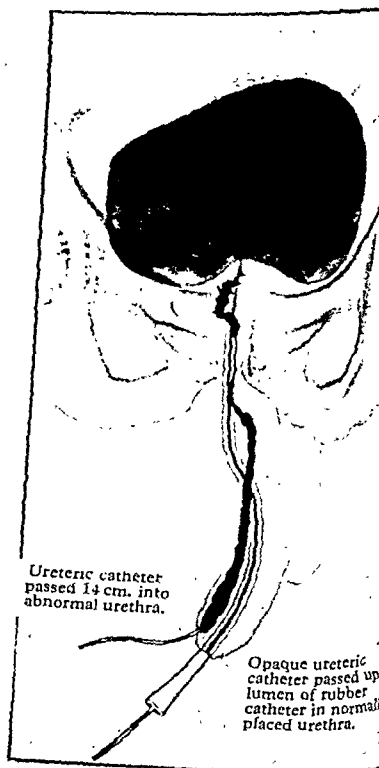


FIG. 3.

L. B., a male patient aged 32, was admitted to the Central Middlesex County Hospital on account of a right-sided epididymo-orchitis of a non-specific nature. On routine examination he was found to possess, in addition to a normally placed urethral orifice, a second smaller aperture opening on the dorsum of the glans (fig. 1). Although no discharge was evident from the normal urethra, the abnormal dorsal orifice emitted a thin white sticky fluid. No specific organisms were detected in this discharge, which had been present for a few days, and there was no history of venereal infection. He stated that he micturated solely through the normally placed aperture, but, that when ejaculation of semen occurred (also from this opening) there was a thin watery discharge from the abnormal channel.

Following the subsidence of the epididymo-orchitis and diminution of the discharge, it was found possible to pass a probe through the small dorsal opening into a sub-cutaneous channel running for a distance of 14 cm. in the dorsal mid-line of the penis. This channel passed beneath the symphysis pubis and seemed to terminate in the prostatic region. Injection of radio-opaque fluid through a ureteric catheter passed into the channel, showed a serpentine continuation at this point, suggestive of a connexion with the right seminal vesicle. Simultaneous urethrocytography was performed through the normally placed urethra, and the combined appearance is shown in the accompanying photograph and diagram (figs. 2 and 3).

From these it will be seen that the normal urethra communicates with the bladder in the usual manner, while the abnormal channel is apparently quite distinct and ends as described above.

The main points of interest in this case appear to be:

(1) The co-existence of right epididymo-orchitis and a discharge only from the dorsally placed aperture, examined in the light of the urethrographic findings.

(2) The anatomical relationship between such dorsally placed channels and the position of the urethra in cases of penile epispadias with sphincteric control.

Owing to the possibility of predisposing the left side of the genital tract to infection, posterior urethroscopy, with a view to establishing the position of the ejaculatory ducts by catheterization, has not been proceeded with.

A somewhat similar case, in which an abnormal dorsal channel communicated, by divarication around the prostate, with both seminal vesicles is recorded by Cruveilhier (1852). A detailed account of further accessory channels is given by Lebrun (1912), and Mackenzie (1916). It is of interest to note that such duplicated "urethras" frequently emit a discharge, the persistence of which may, in some cases, call for extirpation of the track.

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Spinal Anæsthesia and its Effect on a Case of Hydronephrosis and Hydro-ureter.—

Squadron Leader HUGO GRANT, R.A.F.

The treatment of achalasia of the intestine by spinal anæsthesia was first shown to be a possibility by Stabins, Morton and Scott when they found that certain cases of megacolon, in which spinal anæsthesia had been used to gauge the effect of a proposed subsequent sympathectomy, were so much improved following the spinal anæsthesia that the sympathectomy was not required. Telford and Simmons reported 7 cases treated and also 1 case of achalasia of the œsophagus also treated with excellent results. A further case of achalasia of the colon was also reported by Court and Hasler.

Ogier Ward treated a case of bilateral hydro-ureter by pre-sacral neurectomy with excellent results—the contraction persisted eleven months later.

The autonomic nerve supply to the urinary tract is as follows:—

The sympathetic innervation is from the renal, testicular and hypogastric plexuses, and supplies the whole of the urinary tract from kidney to the bladder.

The para-sympathetic through the vagus supplies the kidney parenchyma, and through the sacral para-sympathetic supplies the bladder.

As far as is known there is no para-sympathetic supply to the pelvis or ureter.

An analogy between achalasia of the urinary tract and achalasia of the intestine may be observed in that the obstruction of megacolon is said to be related to the fact that this disorder occurs where the sacral para-sympathetic takes over from the vagus.

When I came across a case of what was considered at first to be achalasia of the renal tract I determined to try the effect of spinal anaesthesia. As will be seen, however, this was almost certainly not a true case of achalasia but the effects were so striking that I feel that it is worthy of record. In this case the spinal anaesthesia was brought up to the level of at least the seventh thoracic nerve and perhaps a little higher, and it was considered likely that most of the sympathetic innervation had been blocked.

T. H., male, aged 33. This man was admitted with a history of three years' painless haematuria. The only relevant thing to note in his past history was gonorrhoea in 1924 from which he had no trouble subsequently. His blood-pressure was 130/80, his blood W.R. was negative and otherwise general examination revealed no abnormality.

An excretory urogram was taken and this showed on the right side a large hydronephrosis with gross dilatation of the calices and pelvis and gross dilatation also of the whole length of the ureter, with a fair-sized oval calculus at the lower end. There was early excretion of the opaque media. On the left side there was also a slight dilatation of the neck of the lowest calix. The appearance suggested achalasia with secondary calculus formation on the right side. On 1.2.43 a spinal anaesthetic was given, 180 mg. of planocaine was used and after twenty minutes there was complete anaesthesia to almost 1 in. below xiphoid and about 4 in. above umbilicus and above that sensation was modified for a further inch. Another excretory urogram was then taken and on the right side the dilatation had disappeared and the kidney and ureter appeared normal except for the calculus. The left ureter was also diminished in size. This excretory urogram was repeated five weeks later and the dilatation was still largely absent. Unfortunately in the interim a cystoscopy had shown the presence of a diffuse papilloma of a malignant type which involved the trigone of the bladder and obscured both ureteric orifices. A cystotomy was later performed and papillomatous formation was found round both ureteric orifices and involving the trigone of the bladder. The right ureteric orifice was partly closed by adhesions. Section of the papilloma showed a malignant change.

Several cases of idiopathic hydronephrosis where the apparent obstruction was at the pelvi-ureteric junction did not respond to spinal anaesthetic.

Comment.—While this is in some respects a record of mis-diagnosis, it has, I think, shown one important thing, and that is that persistent changes may be produced in cases of disordered anatomy of the urinary tract by temporarily interrupting the sympathetic supply, similar to the changes produced by spinal anaesthesia in megacolon.

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Section of Orthopædics

President—W. B. FOLEY, F.R.C.S.

[November 6, 1945]

Treatment of Slipped Upper Femoral Epiphysis

PRESIDENT'S ADDRESS

By W. B. FOLEY, F.R.C.S.

This is a subject upon which, with one exception, I have nothing new to say on the question of ætiology. It is quite certain, I think, that some factor causes weakening of the epiphysal junction. The slip may then be initiated by slight trauma or even by muscle action only and, once begun, is increased by weight-bearing and the fact that many of these patients are overweight. Trauma can never displace the normal upper femoral epiphysis. If it is severe enough it will fracture the neck of the femur leaving the epiphysis undisturbed, and this was demonstrated experimentally by Ollerenshaw and Wood-Jones (1938). The weakening factor is probably a metabolic one since about 70% of these children are either exceptionally tall or overweight and at least 50% show definite evidence of endocrine (probably pituitary) deficiency. The fact that the condition is frequently bilateral and that other epiphyses are occasionally affected, favours an endocrine cause, but there are still the 30% of apparently normal patients with slipped epiphyses to be accounted for.

The exception I mention is a suggestion which comes from Dr. M. Beckett Howorth of New York (1941) in an article reviewing the results of treatment of 62 cases of slipped epiphysis, adding these to a previous review of 70 cases published in collaboration with Dr. A. B. Ferguson (1931). Dr. Howorth has made a detailed analysis of this large number of cases and I shall have occasion to refer to some of his results later. He thinks that the primary condition is a synovitis of the hip occurring during the period of rapid growth, that is between the ages of 9 and 18, and that this lesion causes circulatory changes in and near the epiphysal disc resulting in decalcification and softening. The actual slipping is merely the natural result of weight-bearing or of slight injury to the softened epiphysal junction. He bases this theory on the observations that the early symptoms and signs are those of synovitis and that the capsule can be seen to be swollen in radiographs and in cases where it is opened at operation. The blood sedimentation rate is usually elevated and early radiographs show very constantly juxta-epiphysal decalcification. Gross and microscopic examination of the synovial membrane shows a simple synovitis and cultures have been consistently negative. Howorth thinks the whole picture suggests infection, and explains the negative cultures by technical inability to isolate the organism or virus concerned or to failure to take the culture early enough.

When I came across a case of what was considered at first to be achalasia of the renal tract I determined to try the effect of spinal anaesthesia. As will be seen, however, this was almost certainly not a true case of achalasia but the effects were so striking that I feel that it is worthy of record. In this case the spinal anaesthesia was brought up to the level of at least the seventh thoracic nerve and perhaps a little higher, and it was considered likely that most of the sympathetic innervation had been blocked.

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rotation. The tube is placed centrally above the pelvis. This results in an excellent and strictly comparable lateral view of each hip-joint.

The importance of always having radiographs taken of both hips, even though the symptoms are unilateral, lies not only in getting a normal hip for comparison but in the chance of detecting the presence of an unsuspected early slip on the other side, since the condition is often bilateral. The early slight displacement is nearly always backwards rather than downwards, and so may be undetectable in the A.P. view but quite obvious in the lateral. In the A.P. view, however, there is very constantly seen a well-marked zone of decalcification in the juxta-epiphyseal portion of the metaphysis.

Treatment.—In 1938 Dr. Philip Wilson of New York published a report of 9 cases of early slipping of the upper femoral epiphysis treated by the insertion of a Smith-Petersen tri-flanged pin across the epiphyseal line into the epiphysis, without any preliminary manipulation or attempt at correction of deformity. His criterion of the degree of displacement which could be safely accepted as compatible with normal subsequent function, except for a possible slight limitation of internal rotation, was that clinically there should be free abduction and not more than 10 degrees of fixed external rotation, that the A.P. radiograph should show the upper border of the epiphysis well above the surface of the neck, and that, in the lateral view, the epiphysis should not be displaced posteriorly more than one-third of the diameter of the neck.

After pinning, these patients were kept in bed without splintage or restraint for an average of two weeks and then allowed up on crutches with some raising of the shoe on the sound side. Weight-bearing was allowed in about two months' time. The Smith-Petersen pin was removed at the end of nine to twelve months after insertion, at which time there was radiographic evidence of fusion of the epiphysis in all cases.

The functional results were excellent in every case, the only abnormality being a varying degree of restriction of internal rotation of the affected hip. The maximum shortening was 1 in. in one case in which there was no shortening before operation. There was $\frac{1}{2}$ in. shortening in one other case which had no pre-operative shortening. This absence of material shortening in spite of the early fusion of the epiphysis requires some explanation. The age of closure of this epiphysis has usually been given in the standard textbooks of anatomy as 18 years but Wilson quotes the researches of Cohn (1924), based on radiographic studies, in fixing it at 15 years. Only 17% of the total growth in length of the lower limbs normally takes place at the upper femoral epiphysis, and Wilson suggests that most of this takes place early, and that there is probably very little growth after the age of 12 years till final closure at 15 years. He has also observed that there is usually premature closing of the epiphysis on the opposite side even if there has been no evidence of slipping. These two reasons would account for the absence of any marked inequality in growth in the children aged 12 and over who form the majority of the cases. One might anticipate rather more shortening in the relatively small age-group under 12.

Wilson states that he has made a thorough trial of weight-bearing calipers and ambulatory plasters and rejected them as inefficient and dangerous, since he has seen complete displacement of the epiphysis occur in patients who were being treated by these methods. There are obvious objections to long-continued traction or plaster immobilization in recumbency, if they can be avoided. At the same time it should be understood that these older methods can produce a perfectly good functional result, only they will have to be continued till there is radiographic evidence of fusion of the epiphysis, which may take as long as twelve months. During this period the patient is subjected to more discomfort and interference with normal activity, and is less efficiently protected against further slipping, than when pin fixation is used.

Howarth reports results classified as excellent or good in 39 out of 40 early cases, but used bone slivers passed through drill holes from the neck across the epiphyseal line. He did not use the Smith-Petersen pin because he did not think it hastened fusion of the epiphysis, but that this is not correct is shown by Wilson's cases and my own in all of which there was radiographic evidence of fusion in six months or less. The pin is simpler to use than bone grafts, gives greater security of fixation, and does not require arthrotomy of the hip.

I have only been fortunate enough to get five cases in which the diagnosis was made early enough to conform to Wilson's standard. All these cases were pinned without previous manipulation or traction. The technique is exactly the same as for pinning the fractured femoral neck and presents no special difficulty to anyone with experience

I can confirm these observations from my own cases, i.e. the swelling of the synovial membrane seen at operation, the histological finding of a simple synovitis, the elevation of the blood sedimentation rate in early cases and the constant appearance of justa-epiphysal decalcification in radiographs. We are all familiar with cases of transient synovitis of the hip in much younger children and Howorth's suggestion is an interesting one and would account for the cases with no sign of endocrine disturbance. I should, however, expect an infective synovitis of the hip to produce more muscle spasm than is usually present in early cases of slipped epiphysis, and the decalcification to be more general. Also if an inflammatory ætiology is to be accepted to the exclusion of an endocrine one it is perhaps a less likely though not impossible explanation of the bilateral cases. Except perhaps for the raised sedimentation rate and Howorth's statement that he has observed these changes in hips operated on before there was any demonstrable epiphysal slipping, these findings might be due to traumatic synovitis and secondary to the epiphysal slipping rather than the primary cause of it.

Osteo-arthritis in later life.—It is a matter of common knowledge that osteo-arthritis of the affected hip-joint is an all too frequent sequel of uncorrected or partially corrected epiphysal displacement though it may not manifest itself for several decades. If it be conceded that this type of arthritis is due chiefly, if not entirely, to mechanical irritation caused by the misfit of the deformed femoral head and neck it is obvious that prevention or correction of such deformity as completely as possible should be regarded as a primary object of treatment in the early stages.

The cases can be sharply divided into two main groups, between which is a great gulf fixed, since treatment in the one is so much more satisfactory than in the other: I. Early cases with minimal epiphysal displacement. II. Cases with severe or complete displacement of the epiphysis.

The latter may be further subdivided into (a) acute cases with a short history usually including slight injury and symptoms and signs severe enough to suggest a fracture of the neck of the femur, and (b) those with a long quiet history of gradually increasing pain and deformity.

Group I. Early cases with minimal epiphysal displacement.—This is the most important group because it is the only one in which treatment can be said to be completely satisfactory. Since inclusion in it depends on one thing only—early diagnosis—I should like at this point to stress the paramount importance of diagnosing cases of slipped femoral epiphysis at the earliest possible moment. Those of us who are concerned with the teaching of students or with the post-graduate instruction of general practitioners should take every opportunity of impressing upon them the extreme importance of suspecting this condition in any adolescent of either sex, between the ages of 9 and 18, who is complaining of limping or of pain in the hip or knee. Much emphasis should also be laid on the urgency of admitting these cases to hospital forthwith, or, if this is impossible, of confining them strictly to bed at home pending admission. Once the diagnosis is made, or even suspected but not confirmed by radiograph, all weight-bearing should be forbidden absolutely, since, if continued, there is a grave risk that at any moment the case may pass from the favourable first group to the less favourable second group.

Diagnosis.—Diagnosis in the really early case which is so favourable for treatment may not be at all obvious clinically. Suspicion should be aroused by a history of intermittent limp in an adolescent especially if accompanied by transient pain in hip or knee. Not infrequently pain in the knee is the only complaint but, if unaccompanied by physical signs in that joint, it should be realized that this is referred pain and attention concentrated upon the hip. Muscle spasm may be absent, but there is usually some limitation of internal rotation of the hip and occasionally of abduction and flexion with pain and spasm at the limits of these movements. There will be no pyrexia but the blood sedimentation rate, if estimated, will usually be moderately raised. Diagnosis rests finally on the radiographs and the technique of taking these is most important. Both hips should always be radiographed in such a way that they are shown in exactly comparable positions in both A.P. and lateral views on the same film. This is straightforward as regards the A.P. view, the patient lying with the lower limbs extended at hip and knee, parallel to each other and with the patellæ pointing straight upward unless there is fixed external rotation of the affected hip. The lateral view is obtained by flexing both hips and knees to exactly the same angle and allowing the hips to fall outwards into as much abduction as they will comfortably take and some external

a diagnosis. Subsequently one of two things may happen. Either pain and/or deformity gradually increase until the patient is forced to seek advice and the diagnosis is obvious, or, usually as the result of trauma, pain becomes suddenly very severe, deformity, especially external rotation, marked and the patient is completely disabled and presents the clinical picture of a fracture of the neck of the femur. Radiographs in either group confirm the diagnosis of severe downward and backward displacement of the upper femoral epiphysis. I should like to discuss the treatment of what may be termed the acute case first.

Such cases should be regarded as urgent emergencies and admitted to hospital forthwith, since every hour of delay makes a successful result less probable. The object of treatment is to replace the slipped epiphysis as completely as possible, and if this is successful to fix it with a Smith-Petersen pin. Two closed methods are available for the reduction of the deformity: (1) gentle manipulation; (2) strong continued traction on the limb. Neither of these methods, especially traction, is likely to succeed unless applied within a week, though there are frequent exceptions to this.

Manipulative reduction.—If manipulation is to be followed by immediate pinning, as it should be if successful, the patient is prepared for operation and placed on an orthopædic table with the usual radiographic set-up of 2 portable tubes in position for taking A.P. and lateral radiographs. I usually adopt the Leadbetter (1933) type of manipulation, which gives good results in reducing fractures of the neck of the femur, and, if the slip has been a recent one, reduction often takes place surprisingly easily and completely with slight crepitus. The reduction is checked radiographically and, if sufficiently good, the limb is fixed in abduction and internal rotation and pinning carried out.

If manipulation fails it is useless and harmful to make repeated attempts and no force must be used. Advantage may be taken of the anæsthetic and the prepared state of the patient to insert a Steinmann pin through the lower third of the femur in preparation for the alternative method of strong continued traction.

In both these groups and in those next to be mentioned involving arthrotomy of the hip-joint the after-care is somewhat different to the routine already described for the early cases. The patients are kept longer in bed, usually at least a month, often with a light weight and pulley traction for the first two weeks or so. Walking on crutches without weight-bearing is continued for at least three months and sometimes for as long as six months, depending on the radiographic appearances.

Howorth reported only three partial successes out of 21 cases of manipulative reduction. These cases, however, were not pinned but immobilized in plaster following reduction, and most of them had some permanent limitation of movement. He felt that better results would have been obtained by resting these patients in bed till the condition was quiescent, and then doing sub-trochanteric osteotomy. He advised manipulation in very recent cases only and thought immediate pinning would be preferable to plaster fixation.

In classifying my own cases throughout I use the term "excellent" for patients who are quite symptom free and have either no limitation of hip movement or a few degrees of limitation of internal rotation only. Radiography shows no deformity or evidence of arthritis. Cases marked "good" are leading lives of normal activity with no pain, or only an occasional ache with weather changes, but have definite limitation of internal rotation and possibly also of flexion and abduction. Radiography may show some deformity of head or neck, but no arthritic changes. Results classified as "bad" have pain and/or gross limitation of all hip movement and possibly some fixed deformity. Radiography shows evidence of avascular necrosis or of arthritis.

Eight cases have been treated by manipulative reduction. Three of them were subsequently immobilized in plaster, and in the other five the reduced epiphysis was pinned. In the former group the follow-up period ranges from eight to fourteen years with an average of ten years. Results: Excellent 1; bad 2. One of these subsequently needed arthroplasty of the hip.

The follow-up period of the pinned cases extends from one to seven years averaging five years. Results: Excellent 2; good 2; bad 1.

Total cases 8. Excellent 3; good 2; bad 3 (37%).

The one bad result out of the five pinned cases was the most recent.

of the latter and working with proper facilities especially as regards the necessary radiographic checking during the operation. The after-care consisted of two weeks free in bed, followed by discharge from hospital and two months on crutches with an inch of raising of the shoe on the unaffected side. After this full weight-bearing activity was allowed and the pins were removed at the end of a year or so at which time the epiphysis was fused in every case.

The follow-up period has ranged from one year to seven years with an average of four years. The results have been excellent in every case and compatible with full normal activity. There was $\frac{1}{4}$ in. shortening in one case only and slight limitation of internal rotation in 3 cases.

I am definitely in agreement with Wilson that, given good facilities and a surgeon of some experience in the technique of pinning, this is the method of choice in treating the early case of slipped epiphysis. Under those conditions it is safe, certain and associated with a minimum of hospitalization, discomfort and inconvenience to the patient. The only theoretical objection, the desirability of a second operation to remove the pin, has not proved to be one in practice. There has been no difficulty in getting consent and a fortnight in hospital is usually all that is needed.

CASE I.—M. W. This patient, then aged 14, was first seen in May 1938 and gave a definite history of pain in the left thigh and limp for seven weeks. An occasional transitory limp had been noticed over a longer period. On examination there was



FIG. 1.—Lateral view. Slip does not exceed one-third diameter of neck.



FIG. 2.—After pinning.



FIG. 3.—End-result. Note epiphyseal fusion.

CASE I. (M. W.)

slight limitation of abduction and definite limitation of internal rotation of the left hip. Radiographs showed little deformity in the A.P. view but a characteristic juxta-epiphyseal decalcification, and the lateral view showed the epiphysis displaced posteriorly but not more than one-third the diameter of the neck. It was decided to accept this position and the epiphysis was pinned without any attempt at correction. The patient was discharged from hospital on crutches on the sixteenth post-operative day and the crutches were discarded and weight-bearing allowed two months later. She now works at a job which involves standing all day and engages in every form of athletic activity she wishes without any discomfort. She has a full range of movement of the affected hip in every direction, and $\frac{1}{4}$ in. shortening only.

GROUP II. *Cases with severe or complete displacement of the epiphysis.*—In these cases there is usually, on close questioning, a fairly long history of occasional limping and pain in hip or knee sometimes not severe enough to make the patient consult a doctor at all or, if a doctor is seen, there is insufficiently thorough investigation to make

a diagnosis. Subsequently one of two things may happen. Either pain and/or deformity gradually increase until the patient is forced to seek advice and the diagnosis is obvious, or, usually as the result of trauma, pain becomes suddenly very severe, deformity, especially external rotation, marked and the patient is completely disabled and presents the clinical picture of a fracture of the neck of the femur. Radiographs in either group confirm the diagnosis of severe downward and backward displacement of the upper femoral epiphysis. I should like to discuss the treatment of what may be termed the acute case first.

Such cases should be regarded as urgent emergencies and admitted to hospital forthwith, since every hour of delay makes a successful result less probable. The object of treatment is to replace the slipped epiphysis as completely as possible, and if this is successful to fix it with a Smith-Petersen pin. Two closed methods are available for the reduction of the deformity: (1) gentle manipulation; (2) strong continued traction on the limb. Neither of these methods, especially traction, is likely to succeed unless applied within a week, though there are frequent exceptions to this.

Manipulative reduction.—If manipulation is to be followed by immediate pinning, as it should be if successful, the patient is prepared for operation and placed on an orthopaedic table with the usual radiographic set-up of 2 portable tubes in position for taking A.P. and lateral radiographs. I usually adopt the Leadbetter (1933) type of manipulation, which gives good results in reducing fractures of the neck of the femur, and, if the slip has been a recent one, reduction often takes place surprisingly easily and completely with slight crepitus. The reduction is checked radiographically and, if sufficiently good, the limb is fixed in abduction and internal rotation and pinning carried out.

If manipulation fails it is useless and harmful to make repeated attempts and no force must be used. Advantage may be taken of the anesthetic and the prepared state of the patient to insert a Steinmann pin through the lower third of the femur in preparation for the alternative method of strong continued traction.

In both these groups and in those next to be mentioned involving arthrotomy of the hip-joint the after-care is somewhat different to the routine already described for the early cases. The patients are kept longer in bed, usually at least a month, often with a light weight and pulley traction for the first two weeks or so. Walking on crutches without weight-bearing is continued for at least three months and sometimes for as long as six months, depending on the radiographic appearances.

Howorth reported only three partial successes out of 21 cases of manipulative reduction. These cases, however, were not pinned but immobilized in plaster following reduction, and most of them had some permanent limitation of movement. He felt that better results would have been obtained by resting these patients in bed till the condition was quiescent, and then doing sub-trochanteric osteotomy. He advised manipulation in very recent cases only and thought immediate pinning would be preferable to plaster fixation.

In classifying my own cases throughout I use the term "excellent" for patients who are quite symptom free and have either no limitation of hip movement or a few degrees of limitation of internal rotation only. Radiography shows no deformity or evidence of arthritis. Cases marked "good" are leading lives of normal activity with no pain, or only an occasional ache with weather changes, but have definite limitation of internal rotation and possibly also of flexion and abduction. Radiography may show some deformity of head or neck, but no arthritic changes. Results classified as "bad" have pain and/or gross limitation of all hip movement and possibly some fixed deformity. Radiography shows evidence of avascular necrosis or of arthritis.

Eight cases have been treated by manipulative reduction. Three of them were subsequently immobilized in plaster, and in the other five the reduced epiphysis was pinned. In the former group the follow-up period ranges from eight to fourteen years with an average of ten years. Results: Excellent 1; bad 2. One of these subsequently needed arthroplasty of the hip.

The follow-up period of the pinned cases extends from one to seven years averaging five years. Results: Excellent 2; good 2; bad 1.

Total cases 8. Excellent 3; good 2; bad 3 (37%).

The one bad result out of the five pinned cases was the most recent.

CASE II.—J. W. This child, aged 11, was seen in July 1944 with a typical history of three months' occasional pain and limp and one week's severe pain and inability to walk following a fall. There was an external rotational deformity of 60 degrees, limitation of movement in every direction by muscle spasm, and the blood sedimentation rate was raised to 14 mm. in the hour. The radiograph shows almost complete downward and backward displacement of the epiphysis. Although nine days had elapsed since the presumed time of slipping, reduction was quite easily accomplished by the Leadbetter method without any force at all, and the check radiograph showed this to be complete in both planes. The reduced epiphysis was pinned, the patient was discharged from hospital three weeks later on crutches, and weight-bearing was not allowed for four and a half months. Now, just over a year since reduction, pain, limp and limitation of movement in every direction have recurred and radiographs show failure of epiphyseal fusion, partial extrusion of the pin and recurrence of deformity, and changes in the femoral head suggestive of early avascular necrosis. This was a disappointing result but shows that there is always a risk of ischaemic changes following closed manipulation at the epiphyseal line.

Watson-Jones (1944) attributes these ischaemic changes to over-stretching of the ligamentum teres, already stretched by the backward displacement, causing damage and thrombosis to its vessels, which may be in these cases the chief blood supply left to the epiphysis.

If this is so, as may well be the case, the fair proportion of good results would be those in which, more by luck than by skill, the ligament escapes damage during manipulation.

As one cannot control this result of manipulation and the percentage of cases ending in avascular necrosis is as high as 25% to 30% the method should, I think, be abandoned.

Avascular necrosis is a complication not to be regarded lightly, since it may lead to fibrous ankylosis of the hip or to much limitation of the range of movement and early onset of arthritis.



FIG. 4.—A.P. view. Severe epiphyseal displacement.



FIG. 5.—A.P. view after reduction by closed manipulation and pinning.



FIG. 6.—Deformity of femoral head and ischaemic changes one year after reduction.

CASE II. (J. W.)

Reduction by strong traction.—Skeletal traction by a Steinmann pin through the lower third of the femur is preferred, and the patient may be placed on a frame or the affected limb suspended in a Thomas' splint. There is nothing to be gained by abducting the limb. Weights up to 20 lb. may be used but this strength of traction should not be maintained longer than fourteen days at the outside, as there is some risk of interference with blood supply from the continuous tension of the capsule. If reduction is going to take place it will usually do so within that period. The tendency in this method is to get correction of the downward but not of the backward displacement owing to failure of the epiphysis to rotate. Should it prove successful enough to give an acceptable position the weights are reduced to 10 lb. or less so as to maintain

correction and the reduced epiphysis fixed by a Smith-Petersen pin at the earliest opportunity. Howorth found that this method corrected downward displacement but not backward rotation in most cases. The majority had radiographic changes in the head subsequently suggestive of avascular necrosis and eventual movement was good in one hip only, fair in one and poor in the others. He thinks these poor results were probably due to injury to the capsule and the circulation by the traction and the tension in plaster. I think this is too gloomy a picture of reduction by traction which is the safest method though not always fully effective unless applied early. Howorth's cases were not pinned and he thinks the results would have been better if immediate pinning had followed reduction. Two of my cases out of a number in which this method was tried got a satisfactory reduction in both planes and were pinned. The result in each case was excellent. The cases in which traction failed to reduce were dealt with by other methods but one case, in which strong traction was continued for too long, got a bad result with much restriction of hip movement and changes in the radiograph typical of avascular necrosis.

The following case was bilateral and illustrates well some of the points I made earlier with regard to diagnosis and the necessity of insisting on immediate cessation of weight-bearing.

CASE III.—M. C. This girl, aged 13, was first seen in another department on 3.11.42 with a history of left-sided limp for about two months and of pain in the left hip for the past three days. Radiographs were ordered but not examined at the time and consisted of an A.P. view of the hips only. The patient was instructed to attend for re-examination in a week's time, but weight-bearing was not forbidden. A week later,



FIG. 7.—Left hip. A.P. view.



FIG. 8.—Left hip. After reduction by strong traction and pinning.



FIG. 9.—Left hip. End-result.

CASE III. (M. C.)

when I was asked to see her, there was a fixed external rotational deformity of the left hip, movement was painful and restricted in every direction by muscle spasm, and subsequent radiographs of both hips in both planes showed not only a nearly complete downward and backward displacement of the left upper femoral epiphysis, but an early backward slip of the right upper femoral epiphysis. There had been no symptoms on the right side and no physical signs on examination. There is no doubt that the major displacement of the left epiphysis took place during the week between the two examinations, and could have been prevented if weight-bearing had been forbidden. The patient was admitted to hospital forthwith and it was decided to accept the position of the right epiphysis and this was pinned without any manipulation. Under the same anaesthetic a Steinmann pin was drilled through the lower third of the left femur and strong weight traction, applied for four days, resulted in a satisfactory reduction. This epiphysis was also subsequently fixed by a Smith-Petersen pin. The patient is now free of all symptoms and has no material limitation of movement of either hip-joint.

CASE II.—J. W. This child, aged 11, was seen in July 1944 with a typical history of three months' occasional pain and limp and one week's severe pain and inability to walk following a fall. There was an external rotational deformity of 60 degrees, limitation of movement in every direction by muscle spasm, and the blood sedimentation rate was raised to 14 mm. in the hour. The radiograph shows almost complete downward and backward displacement of the epiphysis. Although nine days had elapsed since the presumed time of slipping, reduction was quite easily accomplished by the Leadbetter method without any force at all, and the check radiograph showed this to be complete in both planes. The reduced epiphysis was pinned, the patient was discharged from hospital three weeks later on crutches, and weight-bearing was not allowed for four and a half months. Now, just over a year since reduction, pain, limp and limitation of movement in every direction have recurred and radiographs show failure of epiphyseal fusion, partial extrusion of the pin and recurrence of deformity, and changes in the femoral head suggestive of early avascular necrosis. This was a disappointing result but shows that there is always a risk of ischæmic changes following closed manipulation at the epiphyseal line.

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Avascular necrosis is a complication not to be regarded lightly, since it may lead to fibrous ankylosis of the hip or to much limitation of the range of movement and early onset of arthritis.



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FIG. 6.—Deformity of femoral head and ischæmic changes one year after reduction.

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through the epiphysial junction and immediate pinning were carried out on 28.1.44. The patient was kept in bed for three weeks, and weight-bearing on the affected hip was not allowed for six months. The present condition, nearly two years after operation, is excellent, since there is no pain, no material restriction of movement and no shortening. Radiographs show a normal position of the femoral head, fusion of the epiphysial junction and no evidence of ischæmic changes.

CASE V.—I. B. This girl, then aged 13, was admitted to hospital on 9.8.40 with a history of intermittent pain in the left hip and knee for eight months, and a great and sudden increase in pain and disability following a fall two weeks before admission. There was an external rotational deformity of 70 degrees and limitation of movement of the left hip in every direction by muscle spasm. Radiographs showed a nearly complete downward and backward displacement of the left upper femoral epiphysis.



FIG. 13.—A.P. view of epiphysial displacement.



FIG. 14.—A.P. view after open reduction and pinning.

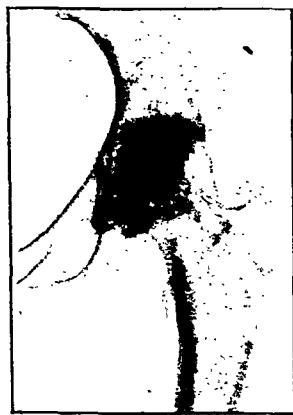


FIG. 15.—Deformity of head and ischæmic changes four years after reduction.

CASE V. (I. B.)

After a short period of rest in bed open reduction through the epiphysial junction followed by pin fixation was carried out on 16.8.40. The patient was allowed up a month later, and walked on crutches without weight-bearing on the affected limb for more than six months. On 2.6.43, three years after the operation, the patient was beginning to complain of pain and radiographs showed loss of joint space, deformity of the head and evidence of avascular necrosis. Pain continued to increase in spite of periods of rest in bed with light traction and removal of the pin and finally arthrodesis of the hip was performed on 9.2.44 and has resulted in satisfactory fusion in good functional position.

The ischæmic changes are probably caused in these cases also by damage to the ligamentum teres due to the leverage on the head during reduction, accentuated by the complete temporary separation at the epiphysial junction and the operative trauma to the capsule.

If reduction by closed manipulation is to be considered unjustifiable, that by open mobilization of the epiphysial junction must be considered even more so, as the results, even with immediate pinning as opposed to plaster fixation, are bad in too high a proportion of cases.

If reduction by strong traction fails and if both closed and open manipulation are to be condemned—as I am afraid they should be—what remains? Light traction may be continued till the epiphysis is fused in the position of deformity and this then corrected by wedge osteotomy of the neck of the femur, or by subtrochanteric osteotomy. The former may be carried out much sooner than the latter since the pin used to fix the fractured neck is made to pass across the epiphysial line into the epiphysis and this prevents further slipping and hastens fusion.

Reduction by open operation.—If strong traction fails to reduce the displacement within fourteen days, this can be effected by open operation.

Open reduction through the epiphysal junction.—This is an attractive operation since it gives almost perfect anatomical correction of the displacement, but it is liable to be followed by ischemic changes in about the same proportion of cases as closed manipulation. It is not a particularly easy operation, is time consuming when followed—as it should be—by pinning with the necessary radiographic checking, and should not be lightly undertaken without first-class facilities. The capsule, exposed by the Smith-Petersen approach, is opened. Only the anterior edge of the epiphysis is visible when the limb is fully externally rotated. A gouge, or in many cases a blunt instrument only, is passed gently between the epiphysis and the neck until the latter moves independently of the former when the limb is rotated. Using the instrument between the bones as a skid and to fix the epiphysis, reduction is effected by an assistant abducting and internally rotating the limb. Reduction is checked by radiographs in 2 planes and, if satisfactory, the capsule and upper aponeurotic portion of the wound are closed and the guide wire and Smith-Petersen pin introduced from the outer aspect of the trochanter in the usual manner.

Howorth reported 17 cases treated by open reduction. 11 of these were immobilized in plaster for ten to twelve weeks after reduction. The follow-up period was two and a half to seven years with an average of five and a half years. There were only 2 good results both of which had a preliminary period of rest in bed with light traction. There were 2 complete failures necessitating arthrodesis in the one case and arthroplasty in the other. The other 6 cases were pinned or screwed after open reduction. Follow-up period averaged two and a half years. 2 were classed as very good, 3 fair and 1 poor. Howorth definitely considered immediate internal fixation with early active movement preferable and advised a preliminary period of rest with light traction in all cases in which muscle spasm was present.

I have treated 9 cases by open reduction through the epiphysal junction. The follow-up period ranged from two years to seven years with an average of three and a half years. Results: Excellent 1; good 5; bad 3 (33%).

The 3 bad results were due to avascular necrosis of the epiphysis resulting in restriction of movement amounting to fibrous ankylosis and in 1 case accompanied by pain of sufficient severity to make arthrodesis necessary.

CASE IV.—C. F. The short term results can be good enough. This patient aged 16 slipped and hurt his right hip fifteen days before admission on 13.1.44. This caused a



FIG. 10.—Lateral view. Complete backward displacement.



FIG. 11.—A.P. view after open reduction and pinning.



FIG. 12.—End-result, two years after reduction.

CASE IV. (C. F.)

limp and a second fall six days later was followed by a marked increase in pain and limping. Radiographs showed a nearly complete slip of the epiphysis especially backwards. Strong traction failed to affect the backward rotation and open reduction

through the epiphysial junction and immediate pinning were carried out on 28.1.44. The patient was kept in bed for three weeks, and weight-bearing on the affected hip was not allowed for six months. The present condition, nearly two years after operation, is excellent, since there is no pain, no material restriction of movement and no shortening. Radiographs show a normal position of the femoral head, fusion of the epiphysial junction and no evidence of ischæmic changes.

CASE V.—I. B. This girl, then aged 13, was admitted to hospital on 9.8.40 with a history of intermittent pain in the left hip and knee for eight months, and a great and sudden increase in pain and disability following a fall two weeks before admission. There was an external rotational deformity of 70 degrees and limitation of movement of the left hip in every direction by muscle spasm. Radiographs showed a nearly complete downward and backward displacement of the left upper femoral epiphysis.



FIG. 13.—A.P. view of epiphysal displacement.



FIG. 14.—A.P. view after open reduction and pinning.



FIG. 15.—Deformity of head and ischæmic changes four years after reduction.

CASE V. (I. B.)

After a short period of rest in bed open reduction through the epiphysial junction followed by pin fixation was carried out on 16.8.40. The patient was allowed up a month later, and walked on crutches without weight-bearing on the affected limb for more than six months. On 2.6.43, three years after the operation, the patient was beginning to complain of pain and radiographs showed loss of joint space, deformity of the head and evidence of avascular necrosis. Pain continued to increase in spite of periods of rest in bed with light traction and removal of the pin and finally arthrodesis of the hip was performed on 9.2.44 and has resulted in satisfactory fusion in good functional position.

The ischæmic changes are probably caused in these cases also by damage to the ligamentum teres due to the leverage on the head during reduction, accentuated by the complete temporary separation at the epiphysial junction and the operative trauma to the capsule.

If reduction by closed manipulation is to be considered unjustifiable, that by open mobilization of the epiphysial junction must be considered even more so, as the results, even with immediate pinning as opposed to plaster fixation, are bad in too high a proportion of cases.

If reduction by strong traction fails and if both closed and open manipulation are to be condemned—as I am afraid they should be—what remains? Light traction may be continued till the epiphysis is fused in the position of deformity and this then corrected by wedge osteotomy of the neck of the femur, or by subtrochanteric osteotomy. The former may be carried out much sooner than the latter since the pin used to fix the fractured neck is made to pass across the epiphysial line into the epiphysis and this prevents further slipping and hastens fusion.

Osteotomy of the neck.—The technique of this method conforms to that just described in all particulars except that no attempt is made to identify and mobilize the epiphysial junction. A wedge of bone with base looking forward or upward according to the predominant deformity, is removed with a fine sharp chisel from the most prominent presenting portion of the neck, the resulting gap closed by abducting and internally rotating the limb, and a Smith-Petersen pin passed across the fracture line and well into the epiphysis. The cut sections of neck are often of slightly different diameter and do not appose perfectly leaving a slight step, but this does not seem to have any material effect on subsequent function and is not apparent in later radiographs.

Of the 9 cases treated in this way 5 were immobilized in plaster following operation, and 4 were pinned. The average follow-up period of the 5 plaster cases was eight years and the results are all classified as good. The follow-up period of the pinned cases is shorter ranging from one to three years, with an average of two years. 1 case is classified as excellent, and the other 3 as good. The majority of these cases have some shortening, but in no case exceeding 1 in. Most of them have some limitation of internal rotation and in some cases of flexion and abduction as well. Restoration of mobility of the affected hip was much speedier and rather more complete in the pinned cases than in those immobilized in plaster after operation.

CASE VI.—D. T. This was one of the cases with a long history (one year) of limp and gradual development of shortening and deformity of the left lower limb. Except



FIG. 16.—Slipped epiphysis and deformity of neck.

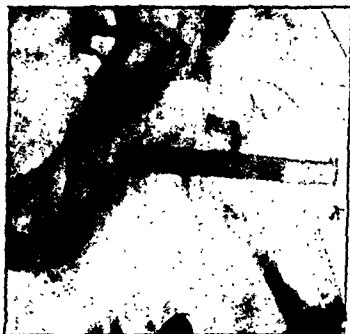


FIG. 17.—Radiograph during operation after wedge osteotomy of neck and pinning.



FIG. 18.—End-result three and a half years after operation.

CASE VI. (D. T.)

for some transient pain and stiffness of the left knee after a fall the patient made no complaint of pain whatever. His age was 15 at the time of admission to hospital on 28.4.42. He had then a fixed external rotation deformity of 45 degrees and flexion and abduction were limited but more from mechanical block than from muscle spasm. Radiographs showed slipping of the epiphysis and marked coxa vara deformity of the neck. It seemed obvious that nothing could be accomplished here by manipulation or traction and that a wedge osteotomy of the neck would be a better procedure than any attempt at mobilizing the already probably partly fused epiphysial junction. This was carried out on 1.5.42 and a pin inserted across the fracture line and well into the epiphysis. The patient was discharged from hospital six weeks later on crutches but weight-bearing was not allowed for seven months. The result is classed as good since the patient is doing heavy work as a farm labourer without any complaint of pain or disability whatever, but he has some limitation of flexion, and marked limitation of internal rotation and 1 in. shortening. Radiographs show a shortened, widened neck with approximately normal angle and some deformity of the head, which may lead to trouble in later life, but at present no evidence of avascular necrosis or of arthritis. This is a fairly typical end-result of this procedure. The absence of ischaemic changes following this operation is probably due to the clean division of the neck allowing correction of deformity without exerting any leverage on the head.

The anatomical correction of deformity is fairly good, but by no means perfect, and though the short-term functional results are good, it remains to be seen whether the long-term results are better than those obtained by subtrochanteric osteotomy.

Subtrochanteric osteotomy.—This operation is much simpler than the others and avoids whatever risk may be associated with arthrotomy of the hip-joint. The division of the bone just below the lesser trochanter is best done by the ball and socket type of osteotomy rather than by removing a wedge, since the former method facilitates the correction of external rotation deformity as well as allowing the necessary abduction at the osteotomy level. It is wise to control the mobile upper fragment by the insertion of a Steinmann pin into the greater trochanter before the bone is divided. This pin may be subsequently included in the plaster spica. The abduction at the osteotomy level has the effect of restoring an approximately correct angle of the neck when the limb is in the normal weight-bearing position and the external rotational deformity is corrected.

Investigation of the results of this operation have been disappointing from lack of information. A number of cases operated upon in 1920-30, the earliest of which I have records, are now of military age and an examination call-up or alternative questionnaire has for the most part failed to produce any response. The reasonable assumption that most of these patients are in the Services might in itself indicate that their functional results are at least fairly satisfactory. Of those I have been able to trace the results are rather mixed. One man fifteen years after operation was working as a gardener and had not been off work because of his hip for ten years, but he complained of some aching in the hip and knee and radiographs showed osteo-arthritic changes. Another man fourteen years after operation was standing long hours in a bakery and only complained of slight pain at changes of weather: radiographs showed deformity but no evidence of arthritis.

In contrast to this good result a third patient three years only after operation had a decreasing range of movement in every direction and evidence of gross arthritic changes in the radiographs. He was not so far complaining of pain. Two other patients eight years from operation both complained of some pain on walking and stiffness after sitting. Radiographs showed deformity but no definite arthritic changes.

I think it would probably be fair to say of subtrochanteric osteotomy that it gives a satisfactory functional result in most cases and delays, if it does not prevent, the onset of mechanical osteo-arthritis by improving the weight-bearing alignment.

A certain number of cases in 1920-30 were treated by a short period of traction in bed followed by the wearing of a caliper splint for a year or longer—or by a caliper only. I have only been able to trace a few of these cases and again the results are rather mixed. The longest follow-up was twenty-three years from the time of discarding the caliper. This man was in the county police and had no complaint of pain or stiffness for the past six or seven years. He had 10 degrees of fixed external rotation and no internal rotation movement therefore, but other movements were free and there was 1 in. of shortening. Radiographs showed deformity but no arthritic changes.

By contrast another man, sixteen years after discarding the caliper, complained of pain in the left knee and hip which limited activity. He had fixed external rotation deformity of 45 degrees and considerable limitation of all other movements of the hip. Radiographs showed deformity, loss of joint space and arthritic changes. Another man sixteen years after treatment was working as a market gardener and on his feet all day long without complaint. Abduction and internal rotation were limited and there was 1 in. of shortening. Radiographs showed much deformity but no definite arthritic changes.

A fourth man, also sixteen years after cessation of treatment, was a concrete worker and complained of pain in the hip only when he worked extra hard, and of stiffness after sitting for long. No recent radiograph of this case was obtainable.

These results, as far as they go, show that hips treated conservatively without operation can function satisfactorily for as long as approximately two decades, and that uncorrected deformity may exist for many years without radiographic evidence of arthritic changes. It is an indication that there must not be too much striving after anatomical perfection if it involves any risk of serious early impairment of function.

SUMMARY

The ideal, at which we should all aim, is early diagnosis of slipping of the upper femoral epiphysis before there is sufficient deformity to need correction. A slight backward rotation can be accepted as it will not materially affect subsequent function.

Osteotomy of the neck.—The technique of this method conforms to that just described in all particulars except that no attempt is made to identify and mobilize the epiphysial junction. A wedge of bone with base looking forward or upward according to the predominant deformity, is removed with a fine sharp chisel from the most prominent presenting portion of the neck, the resulting gap closed by abducting and internally rotating the limb, and a Smith-Petersen pin passed across the fracture line and well into the epiphysis. The cut sections of neck are often of slightly different diameter and do not appose perfectly leaving a slight step, but this does not seem to have any material effect on subsequent function and is not apparent in later radiographs.

Of the 9 cases treated in this way 5 were immobilized in plaster following operation, and 4 were pinned. The average follow-up period of the 5 plaster cases was eight years and the results are all classified as good. The follow-up period of the pinned cases is shorter ranging from one to three years, with an average of two years. 1 case is classified as excellent, and the other 3 as good. The majority of these cases have some shortening, but in no case exceeding 1 in. Most of them have some limitation of internal rotation and in some cases of flexion and abduction as well. Restoration of mobility of the affected hip was much speedier and rather more complete in the pinned cases than in those immobilized in plaster after operation.

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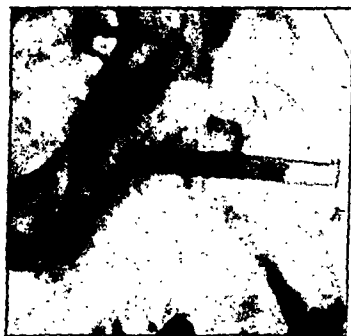


FIG. 17.—Radiograph during operation after wedge osteotomy of neck and pinning.



FIG. 18.—End-result three and a half years after operation.

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Section of Comparative Medicine

President—W. A. POOL, M.R.C.V.S.

[December 21, 1945]

DISCUSSION ON THE METHODS TO BE EMPLOYED IN ERADICATING TUBERCULOSIS OF BOVINE ORIGIN FROM THE HUMAN AND ANIMAL POPULATIONS

Mr. T. Dalling: *The control of bovine tuberculosis.*—The incidence of bovine tuberculosis in cattle in this country is high and its control must take a prominent place in the freeing of our herds from disease. Control and finally complete eradication of bovine tuberculosis are of major importance because of the effect of the infection from cattle sources upon the health of the human population as well as from the point of view of the general health of the cattle herds throughout the country. Attention in the past has been focused largely on the damage done to the human being from tuberculous infection of cattle origin. This has been all to the good and it is right and proper that we should view the problem of the tuberculous bovine from that angle: we must not forget, however, the large economic loss to farmers and to the State which arises from the high incidence of the infection in cattle herds and the comparative national prosperity that would accrue in the livestock world if tuberculosis could be well controlled or eradicated. The health of cattle has a definite relationship to the incidence of tuberculous animals in the herd: when a herd is freed from tuberculous infection the general health, apart from infectious diseases, improves markedly with consequent improvement in milk and meat yields.

In discussing methods of control and eradication due consideration must be given to circumstances pertaining in different countries; hence, it may be found that the same methods which were used in countries such as America and Finland, countries in which tuberculosis eradication is fully or almost fully completed, cannot be adopted in Great Britain.

Tuberculosis is spread among cattle mostly by direct contact from animal to animal: our methods of husbandry and housing are such that the presence in a herd of an animal excreting virulent tubercle bacilli will cause the spread of infection. It is noteworthy that the incidence of tuberculosis in a herd often varies with age-groups of animals, young stock which do not normally come into contact with adult animals having the lowest incidence: in many breeding herds in which infected animals are present the young stock is free from tuberculosis. Other methods of infection exist; for example, there is an increasing amount of evidence that bovine tuberculosis may be transmitted from an infected human being to cattle. The incidence of pulmonary tuberculosis in adult human beings due to infection with the bovine type may be greater than was at one time thought; it follows that "open" human infections may be of importance in the transmission of infection to cattle and due consideration must be given to spread by such means.

Control and/or eradication of tuberculosis in cattle may be attempted by several different methods. The following are examples: (a) The segregation of healthy calves

In treating these early cases the use of the Smith-Petersen pin does seem to be an advance on older methods since it shortens hospitalization, simplifies after-care and accelerates the curative factor of epiphysal fusion without causing material shortening of the limb. The functional results have been uniformly excellent.

When the epiphysal displacement has passed beyond acceptable limits, correction is desirable to prevent the coxa vara deformity which is liable to lead to the development of mechanical osteo-arthritis in later life. The better the anatomical correction, the better should be the prospect of prevention of arthritis, but if the chosen method causes ischæmic changes leading to severe restriction of hip movement the price must be considered too high. It is better to accept some uncorrected deformity, modified perhaps by the relatively simple operation of subtrochanteric osteotomy, which may result in a mobile and comparatively painless hip for two or three decades before arthritis develops, if it does at all, than to obtain a perfect anatomical correction but a stiff hip-joint within five years of manipulative reduction.

It seems clear from the results I have given, both English and American, that correction of epiphysal displacement by closed and still more by open manipulation at the epiphysal junction does entail a definite risk of causing avascular necrosis of the femoral head, and though the anatomical correction is almost perfect and many of the short-term functional results are good, I think that both these methods should be condemned.

Reduction by strong traction is safe if not maintained too long but, unless applied early, is not always effective in reducing displacement especially the backward rotation. If successful it should be followed by immediate pinning. If it fails and the deformity is considered severe enough to need correction this may be effected by wedge osteotomy of the neck of the femur and pinning, or at a later date, after fusion of the epiphysis has occurred, by subtrochanteric osteotomy. The comparatively short-term results of the former operation in my small series have been functionally good and no case has shown evidence of avascular necrosis of the femoral head. The anatomical correction is rather better than that obtained by subtrochanteric osteotomy. To justify the operation, however, it will have to be shown that the long-term results, especially as regards prevention of mechanical osteo-arthritis, are definitely better than those resulting from the simpler extra-articular operation.

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Section of Comparative Medicine

President—W. A. POOL, M.R.C.V.S.

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Control and/or eradication of tuberculosis in cattle may be attempted by several different methods. The following are examples: (a) The segregation of healthy calves

from tuberculous adults and their rearing under conditions which prevent them from becoming infected. (b) The detection of all infected animals and their disposal, healthy, non-infected animals being maintained during the clean-up under conditions which will preserve their freedom from infection. (c) The creating by vaccination of a resistance or immunity to bovine tuberculosis. (d) The treatment (curative) of infected cattle which are considered worth treating.

It may be that a combination of two or more of these methods should be considered.

To attempt, as has been suggested, to slaughter all known infected cattle would so deplete the country of milk-producing stock that serious consideration can never be given to it. Measures will have to be adopted whereby the disease is controlled to a greater extent than it is to-day with the object in view of its final eradication. This will mean a long programme. Attempts are even now being made to control tuberculosis on a herd basis; this can, however, be carried out only in self-contained herds in which movement of stock is very limited. It will be necessary to extend the system of tuberculosis control to areas, some small, as a beginning, with a gradual linking of the areas until the country is covered. Removal of infected cattle from herds and areas is the important break in the further infection of the animals in question; their disposal, however, is of even greater importance. Mr. Ritchie will refer more fully to this point. There may be something to be said for Sir William Savage's view that there should exist special herds in which infected cattle can be collected and where they can be maintained so long as they are of economic value. It may be that an extension of the herd scheme which he has suggested to areas would provide an answer to the question of disposal of infected animals.

No matter which method of control is ultimately decided upon, the diagnosis of the infected animal is all-important. The present method is by the use of tuberculin, injected intradermally, with the reading of the resulting reaction some days later. The diagnosis of bovine tuberculosis must depend on the use of tuberculin; up to the present we have not been able to devise any more reliable method. The type of tuberculin which we are using to-day differs very considerably from that used a few years ago. It is now a comparatively simple procedure to prepare purified protein derivative (P.P.D.) which contains at least 90% of tuberculo-protein produced during the growth of tubercle bacilli on liquid medium which itself contains no protein; this is the so-called "synthetic medium" in which asparagine is the source of nitrogen. By simple chemical treatment of the filtrate the purified tuberculo-protein is made available.

Tuberculin testing is a somewhat complicated procedure for we have now much evidence that no tuberculin yet prepared is specific for the diagnosis of one single type of tuberculous infection, and, further, that cattle can become sensitized by a variety of agents which renders them reactive in different degrees to different "tuberculins". In discussing tuberculin we have to consider the acid-fast group of organisms as a whole. We find in studying the "tuberculins" produced from them that each has both a homologous and a heterologous specific factor. For purposes of discussion tuberculins can be divided into groups of which the most important from our point of view are those derived from tubercle bacilli of mammalian and of avian origin. Tuberculins from human and from bovine strains of tubercle bacilli contain tuberculo-protein rich in mammalian specificity and lower in avian specificity. The relationship factor is roughly 1 to 20-40. Within the mammalian group the relationship between the specific factors of human and bovine strains is roughly 1 to 2. Thus, it would seem a comparatively simple matter to differentiate between bovine and avian sensitivity by the use of the respective tuberculins. Unfortunately this does not hold good; cattle are relatively insensitive to any tuberculin when compared with the sensitized guinea-pig or the human being and comparatively large amounts of tuberculo-protein are required to elicit any reaction in them no matter what their state of sensitivity. It will therefore be evident that the differences in the reactions produced by these two tuberculins has led to some confusion. There has, however, been worked out a scheme of testing whereby reasonable accuracy is obtained especially when the herd-testing history is known.

Modern tuberculins are tested for potency and specificity and are compared with "standards". Sensitized guinea-pigs are used for such work, sensitization being accomplished by actual infection of the animals with specific strains of *M. tuberculosis*.

One great advantage in using P.P.D. is that it is possible with a minimum of trouble to ensure that tuberculin of similar potencies and specificities can be used at all times and thus operators can compare results on the same animals no matter at what intervals the successive tests are carried out.

Work is in progress in attempts to increase the specificity of tuberculin. There are indications that by chemical means it may be possible to prepare more highly specific tuberculins: until such preparations are available it will be necessary to continue to use the so-called "comparative" test, i.e. the simultaneous injection of mammalian and avian tuberculins.

Some attention has been given to the immunization of cattle against tuberculosis and to its place in the control of tuberculosis. Although our work has progressed within recent years we have not yet reached the stage when we can give a definite opinion on the place of vaccination in the control of the disease in the field. It will be recalled that the B.C.G. culture of bovine tubercle bacillus, elaborated some years ago by the French workers, has been the subject of experimental research in many countries and that workers in this country have also included it in their studies. We have already reported at meetings of this body and in the scientific press the results of laboratory and semi-field experiments in which it was shown that repeated intravenous injections of a suspension of the culture set up a resistance to artificial infection with bovine tubercle bacilli at a later period. It became necessary to examine the use of the cultures under field conditions and for this work the Agricultural Research Council organized a field trial which includes about 100 farms. The main object of the trial is to ascertain in how far the use of B.C.G. vaccine can assist a farmer in the changing of his herd from one containing many cattle infected with tuberculosis (as shown by their being positive reactors to the tuberculin test) to one free from tuberculosis. The trial is of a simple nature. A survey of the incidence of tuberculosis in the whole herd is made (tuberculin testing) before the herd is accepted for inclusion in the trial. Only herds in which the incidence of tuberculosis is high are selected and in which the young stock are comparatively free. Only calves and young unbred stock which fail to react to the tuberculin test are included in the trial.

Every six months a dose of the culture suspension is injected intravenously. As the young stock reach maturity and are in milk production they are brought into the milking herd and an equal number of the original cows are disposed of: hence, in a period of time which varies with the size of the herd the milking-herd consists entirely of vaccinated animals. At this stage vaccination ceases. It is hoped that by this means farmers who are not in a position to adopt other means of clearing their herds of tuberculous infection will be able to have a clean herd in a minimum of time. An objection to the method is that the injection of the culture is followed by a sensitivity to tuberculin; our finding, however, is that the sensitivity to mammalian tuberculin is of comparatively short duration and that within 9 to 12 months following the cessation of vaccination, vaccinated animals are considered free from bovine tuberculosis so far as the tuberculin test is concerned. It is as yet too early to give an opinion on the usefulness of this method as an adjunct to controlling tuberculosis; we shall not be in a position to make any statement for probably two years. We can at this stage, however, say that a few herds in the trial now consist entirely of vaccinated animals and that they have been accepted as T.T. herds under the Milk Designations Order.

The use of B.C.G. vaccine is not without some risk. We have experienced some peculiar "reactions" following the injection of the vaccine, a few of which have been alarming. While we were prepared to find some disturbances of health and actual deaths immediately following the injection of the culture, we were somewhat surprised to meet a peculiar delayed reaction in which respiratory distress, marked emaciation and lameness were prominent and occurred at any time up to three or four weeks following an injection. These reactions are not confined to the first injection but have been noted following injections at all stages of the trial. The number is comparatively small and not confined to one farm or group of farms but may affect one or more animals in different parts of the country.

Preliminary experiments indicated that suspensions of the vole acid-fast organism injected intravenously into cattle gave rise to a resistance to bovine tuberculosis of an order equal to or even higher than that obtained with B.C.G. Work with this organism is still in progress and the results are not yet sufficiently advanced to make any further statement on its usefulness as an immunizing agent. It will be some little time before the experiments warrant a field trial.

References to the literature show that many attempts are being made to evolve methods of effecting cures of bovine tuberculosis by the use of chemical compounds. If success attends the investigators' work by the finding of suitable products for this purpose there is little doubt that a high place will be found for such treatments in human medicine. Doubtless, also, there would be some who would advocate similar treatment for affected cattle. There must be, however, in the minds of many of us some grave doubts of the

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No matter which method of control is ultimately decided upon, the diagnosis of the infected animal is all-important. The present method is by the use of tuberculin, injected intradermally, with the reading of the resulting reaction some days later. The diagnosis of bovine tuberculosis must depend on the use of tuberculin; up to the present we have not been able to devise any more reliable method. The type of tuberculin which we are using to-day differs very considerably from that used a few years ago. It is now a comparatively simple procedure to prepare purified protein derivative (P.P.D.) which contains at least 90% of tuberculo-protein produced during the growth of tubercle bacilli on liquid medium which itself contains no protein; this is the so-called "synthetic medium" in which asparagine is the source of nitrogen. By simple chemical treatment of the filtrate the purified tuberculo-protein is made available.

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milking cow as far as possible, the incidence can be greatly reduced. In such a herd it will be recognized that removal of clinically infected cows, particularly those giving tuberculous milk, is of very considerable value.

In this country, it is usually found that in a herd which at its first test shows no reactors to the tuberculin test the method of management has closely followed the one outlined above. Such herds are not so frequently found nowadays, as many of them have already been tested and have become recognized as tubercle-free herds. It is still very common, however, to find a herd in which there is a high incidence of disease among the cows whereas the young stock are practically all free of infection. Owners of such herds can often be persuaded to remove all the cows from the herd, to replace them by cows from attested herds, and thus establish a clean herd, as it were, overnight. The non-reacting young stock are retained. In one or two parts of the country this practice is frequently followed, and if care is taken to clean and disinfect the cow sheds and buildings thoroughly before the new cows are introduced, remarkably good results have been seen at subsequent tuberculin tests. Even in fairly valuable pedigree herds, owners are often not averse to this method as they are able, by retaining their non-reacting young stock, to maintain breeding lines which may be of considerable value to them. It has been found that the subsequent history of the herds as regards reactors is invariably good and the owners maintain that the financial benefits from this rapid eradication are considerable. In this type of herd it is possible to eradicate the disease without immediately disposing of the reactors. Where an owner has two sets of farm buildings, it is usually a simple matter to segregate the non-reactors from the reactors. The reactors are kept in separate buildings and are disposed of as opportunity offers and replaced by non-reactors and their shed can come into use for free stock after suitable preparation. By segregation of non-reactors and reactors on the same farm or even in the same shed this procedure may also be followed but the difficulties are greater. When this method of segregation of reactors and retention of all non-reactors is followed, the subsequent history of the herd is seldom so good; at the herd retests, which should be done some sixty days after the initial test, it is not uncommon to find a fairly high percentage of reactors among the non-reactor group. A few reactors will be found in many herds at the third or even subsequent herd tests, and I have known cases where, as testing proceeded, all the non-reacting cows at original test have eventually been removed as reactors.

A possible modification of this method may one day become available if either of the methods of vaccination at present under test proves satisfactory. An effective vaccine has a limited practical application, however. It is of no value in flying herds, which are often most heavily affected; if calves have already become infected, for instance from tuberculous milk, its full advantage is lost.

The first test of the herd is of prime importance; unfortunately, it is usually found to be the most unreliable. It was in herds tested for the first time that we found so many tuberculous animals which failed to show reactions at the normal times of observation. Late positive reactions have not been so often encountered since the potency of the tuberculin has been increased, but it is still not uncommon to find, in animals tested for the first time, that no response to tuberculin is seen until the ninety-sixth hour after injection. It is essential in the employment of the tuberculin test in cattle to recognize the fact that it has greatest value if it is employed as a herd test. This is more than ever important in assessing the results of the comparative test, which has already been mentioned. In the initial test of a herd, the first essential is to be sure that all clinical cases which can possibly be recognized have been removed, to avoid the tremendous risk of retaining as a non-reactor the grossly diseased animal which does occasionally fail to react. The results of the test should then be assessed on the basis of deciding the fate of the animals in groups designated with reference to their common housing, grazing and general contact. If a clinical case has been found in any group showing a high percentage of reactors, say, 50%, it is unwise to retain any of the non-reacting animals in that group and, indeed, it is probably good practice to recommend to an owner to dispose of the non-reactors in a group of cattle unless there are less than 20% reactors in that group. A number of reactors among young calves, for instance, almost invariably indicates that a cow in the herd is excreting tubercle bacilli and the calves have become infected from her milk; if this cow has not already been recognized, she should be sought for, and it is unwise to confine the search to the reacting cows entirely, although she will usually be found among them. Having decided which animals are to be removed and how the effort to establish a free herd is to proceed, it is essential to carry out periodical tests of the non-reactors, whether the reactors have all been removed from the farm or are in isolation on some portion of it.

place which even the perfect curative treatment could occupy in the control of tuberculosis in cattle. Our policy must be one of prophylaxis rather than curative treatment, for a minimum of imperfectly treated animals in a herd or an area would be fatal to any control or eradication scheme. We feel strongly that too great emphasis must not be given to the adoption of curative methods and that plans must be laid in other directions.

No matter which method or combination of methods is to be adopted the eradication of bovine tuberculosis from the herds in this country must of necessity be a long-term policy. That, of course, is no reason why, after careful planning, a beginning should not be made on a fairly wide scale at an early date. We must take due notice of the fact that the large majority of calves are born free from tuberculous infection and can be so maintained, that there are already in the country areas in which the incidence of tuberculosis is quite low, and that for all practical purposes this country is self-contained so far as cattle are concerned.

The points for discussion, as I see them, are the following: (1) How to ensure that young, healthy stock can be kept free from tuberculosis; (2) the possibilities of creating areas free from the disease, of maintaining healthy cattle in them, and of extending such areas until finally the whole country is covered; (3) the disposal of infected cattle; (4) improvements in our present methods of diagnosing tuberculosis; (5) vaccination as an adjunct to methods of control and eradication.

Mr. J. N. Ritchie: Where success in eradication of tuberculosis in cattle has been achieved, the tuberculin test and disposal of reactors has been the method employed.

Some form of intradermal test is used in practically every country nowadays. In Great Britain, we use the double intradermal test, and since 1940 have injected two tuberculins, mammalian and avian, into selected sites in the neck. By comparing the reactions produced by the two tuberculins, it has been found possible to recognize those animals sensitized by the bovine type of organism and those sensitized by some other related organism; this is of great practical importance, since only the bovine type organism produces progressive disease in cattle. This comparative test has been found extremely useful when used as a herd test; for testing individual animals it has less value, but it is not alone among tuberculin tests in this respect.

We recognize five organisms which sensitize cattle to mammalian tuberculin: *Mycobacterium tuberculosis* of bovine, human and avian types, *Mycobacterium johnei*, and an acid-fast organism associated with lesions in the skin. There is some evidence that the actinobacillus may also sensitize and a suspicion that other organisms may also be involved. It is not difficult to recognize the reactor sensitized by the avian type organism or by the Johne's bacillus: it is more difficult to recognize the reactor sensitized by the organism associated with skin lesions unless the lesions have been observed. It is extremely difficult to differentiate the reactor sensitized by the human type from the one sensitized by the bovine type of tubercle bacillus. When there is a suspicion from the history of the herd, and of the people who are in close contact with it, that a human source of infection is present, it may be necessary to retest reactors even though the test suggests that a bovine type of organism is involved. The sensitization from the human type of organism is usually comparatively fleeting and this fact may often allow a differentiation at the time of retest. However, it must be remembered that infection from a human source is not necessarily from the human type of organism but may well be from the bovine type. Some form of comparative test must be used until a more specific tuberculin can be produced.

Removal of clinical cases from a herd, unassociated with other efforts of control, makes only a slight contribution to the elimination of infection.

Removal of clinical cases is, of course, of value from the public health point of view and the efforts which have been made to remove clinical cases have been aimed mainly at reducing the weight of infection in the milk supply. In this connexion, sampling of bulk milk for biological test and further investigation on the premises supplying positive samples might well be increased with advantage.

Care in herd management based on recognition of the fact that very few calves are born infected can contribute greatly to success in control within the herd. Only a small percentage of young cattle is infected and, in general, it is at the stage when a milking heifer is introduced to the dairy herd that she picks up her primary infection. Where care is taken to maintain the young stock separate from the cows and segregate the young

already been done, and the numbers of animals slaughtered under the Tuberculosis Order in each county since 1925. In 1938-39 survey tests were made on selected self-contained herds. In all, 364,286 cattle were tested and revealed 13% reactors. Because of the method of selection of the herds, and the fact that more testing was done in districts where good results were obtained, this figure cannot be taken as a reflex of the position throughout the country but, if the figures are studied more closely county by county, and in conjunction with the other factors which can be taken into account, a much more accurate estimate can be reached. The survey tests in England gave a percentage incidence of reactors of 14.1%. In eight counties showing an incidence of reactors of over 25%, 14,300 cattle were tested from a population of 1,148,646; whereas where less than 10% reactors were found 51,315 cattle were tested from a population of 1,305,450. This in itself suggests that the incidence figure for the country is too low. Adjusting the figures for each county in the light of the numbers slaughtered under the Tuberculosis Order and the numbers now in tubercle-free herds I have reached a figure of 20% as the approximate incidence of reactors in England. In Wales, the survey test showed 4.1% reactors among 116,082 cattle tested. Some counties showed an extremely low incidence and in them there are now large numbers of attested herds so that this factor has not reduced the incidence markedly from the survey test figure. On the other hand, there are one or two counties with large numbers of flying herds with a heavy infection and by adjustments on a county basis the incidence appears to be in the region of 7.5%. The herds surveyed in Scotland showed 23.1% reactors. The indication of the weight of infection county by county as revealed by the Tuberculosis Order figures very closely conforms with the test survey figures. However, the response to the Attested Herds Scheme in Scotland has been good and in some counties extremely so; there are high percentages of attested cattle in several counties where the incidence was high as revealed by the survey test and consequently the incidence in the country has been considerably reduced since the time of the survey. It is now probably about 14%.

Throughout Great Britain I have estimated the percentage of reactors to be between 17 and 18% of all the cattle. This represents a probable 30 to 35% infection among cows, so that in view of recent reductions in incidence by the eradication of infection from many herds, the estimate of 40% infection among cows may not have been very high at the time it was made.

Sir William Savage (*in absentia* read by Dr. A. Haddow): While the eradication of tuberculosis in bovines is essentially a veterinary problem the fact that many cases of tuberculosis in man are of bovine origin makes us, on the medical side, vitally interested in the problem.

Certain facts, I suggest, are incontrovertible. One is that tuberculosis in cows in Great Britain is very extensive, although irregularly distributed. Secondly, all measures, apart from the use of tuberculin to obtain tuberculosis-free herds, are unscientific in conception, and so doomed to failure. Thirdly, any system of eradication of tuberculosis in bovines must be a long-term one and, even if completely successful eventually, cannot in the meanwhile prevent much milk infection with tubercle bacilli and much human disease if the milk or milk products are consumed raw. Knowing that the price of delay is a heavy annual toll of human deaths from bovine tuberculosis and a still larger toll of crippling disease, the various bodies representing medical and Public Health interests have passed resolutions insisting upon the urgent need for the compulsory pasteurization of our milk supplies. Prolonged and detailed investigations have established that pasteurization causes no material damage to the nutritive qualities of milk and that when effectively carried out it renders milk free from the risk of carrying pathogenic bacteria. The only difference of scientific opinion which exists is whether the whole of the milk supply should be pasteurized, or if an exception should be made for milk from herds free from tuberculosis. In view of the risks from other pathogenic bacteria in milk those who hold the first view are scientifically justified, but since the risk from the tubercle bacillus is so much the greater many of us are content to permit, at least for the present, milk from tubercle-free herds to be sold raw. This compromise should facilitate the eradication of bovine tuberculosis.

In the eradication of tuberculosis in bovines, the chief problem is the "reactor". Four methods have been considered. One is to slaughter without compensation, but as it is obviously unfair and impracticable it needs only mention. Another is to slaughter and

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One method that commends itself is eradication of the disease from defined areas of the country, and for this method authority is contained in the Agriculture Act, 1937, by which the Minister may declare eradication areas and slaughter reactors when a substantial proportion of the cattle in an area is free from disease. There are many advantages in area eradication. The work of supervision and testing the 20,000 attested herds in this country has now become extremely heavy. On the average, the herds are tested one and a half times per annum, and if eradication is to proceed it would be a colossal task to maintain that frequency of testing throughout all the herds; at present, because of the risks of reinfection, this frequency must be maintained, but it is already being shown that where large numbers of herds contacting each other in a district are attested, the percentage of reactors is lower because the risks of reinfection are less. We have the American experience where herds in which no reactors are found are tested at from three to six years. If we can establish tubercle-free areas we can, after the initial stages, increase the interval after a clear test from the present twelve months to three years, and thus reduce the amount of work and release staff for districts which are in need of it. In a free area, it would be much easier for herd owners who at present have to take a variety of careful precautions against neighbouring infected herds. It would also be possible to allow free inter-herd movement of cattle inside the area instead of requiring that all movements must be on the authority of a permit issued to the owner.

The 20,000 attested herds in Great Britain, comprising approximately 750,000 cattle, represent about 9% of the total cattle. In England 4.24%, in Wales 19.52%, and in Scotland 21.8% of cattle are in attested herds. In England, the highest county figures are 15.4 in Berkshire, and 14.1 in Surrey, with only two other counties showing over 10%. In Wales, the highest figures are Carmarthen 49.6, Cardigan 48.3, Merioneth 34.3, Pembroke 28.8, with two other counties over 10%. In Scotland, Bute has 75.4% attested cattle, Ayr 66.3, Kirkcudbright 46.5, Dumfries 45.2, Lanark 43.5, three other counties over 30%, three over 20%, and seven over 10%. There are some districts in Scotland and Wales, then, which have progressed sufficiently to suggest that, on the consideration of the weight of infection in them, area eradication might reasonably commence in a comparatively short time. It would be necessary, before declaring areas, however, to ensure that this method was adopted with a reasonable prospect of development from one area to another, until gradually the whole country was covered. It would be necessary to ensure that the areas were large enough to provide within them all the facilities, such as markets for the owners in the area, and also that they left such facilities still available to owners who remained outside the area.

The incidence of tuberculosis in cattle in Great Britain cannot be closely estimated, as there is not sufficient evidence of tests of large numbers of cattle throughout the country. The most commonly quoted figure is that 40% of cows are infected, but that figure is based largely on slaughterhouse returns, and is certainly too high, but it was estimated, of course, when there were very few tubercle-free herds in this country. With the evidence which is available, I have attempted to reach an estimate of the incidence. I have taken into account the number of cattle, approximately 750,000, in attested herds and the number, approximately 140,000, in T.T. herds which are not attested (these latter cattle show a percentage of reactors of about 2%), the evidence of survey testing which has

already been done, and the numbers of animals slaughtered under the Tuberculosis Order in each county since 1925. In 1938-39 survey tests were made on selected self-contained herds. In all, 364,286 cattle were tested and revealed 13% reactors. Because of the method of selection of the herds, and the fact that more testing was done in districts where good results were obtained, this figure cannot be taken as a reflex of the position throughout the country but, if the figures are studied more closely county by county, and in conjunction with the other factors which can be taken into account, a much more accurate estimate can be reached. The survey tests in England gave a percentage incidence of reactors of 14.1%. In eight counties showing an incidence of reactors of over 25%, 14,300 cattle were tested from a population of 1,148,646; whereas where less than 10% reactors were found 51,315 cattle were tested from a population of 1,305,450. This in itself suggests that the incidence figure for the country is too low. Adjusting the figures for each county in the light of the numbers slaughtered under the Tuberculosis Order and the numbers now in tubercle-free herds I have reached a figure of 20% as the approximate incidence of reactors in England. In Wales, the survey test showed 4.1% reactors among 116,082 cattle tested. Some counties showed an extremely low incidence and in them there are now large numbers of attested herds so that this factor has not reduced the incidence markedly from the survey test figure. On the other hand, there are one or two counties with large numbers of flying herds with a heavy infection and by adjustments on a county basis the incidence appears to be in the region of 7.5%. The herds surveyed in Scotland showed 23.1% reactors. The indication of the weight of infection county by county as revealed by the Tuberculosis Order figures very closely conforms with the test survey figures. However, the response to the Attested Herds Scheme in Scotland has been good and in some counties extremely so; there are high percentages of attested cattle in several counties where the incidence was high as revealed by the survey test and consequently the incidence in the country has been considerably reduced since the time of the survey. It is now probably about 14%.

Throughout Great Britain I have estimated the percentage of reactors to be between 17 and 18% of all the cattle. This represents a probable 30 to 35% infection among cows, so that in view of recent reductions in incidence by the eradication of infection from many herds, the estimate of 40% infection among cows may not have been very high at the time it was made.

Sir William Savage (*in absentia* read by Dr. A. Haddow): While the eradication of tuberculosis in bovines is essentially a veterinary problem the fact that many cases of tuberculosis in man are of bovine origin makes us, on the medical side, vitally interested in the problem.

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Sir Merrik Burrell: The theoretically fine idea of forming tuberculosis-free areas was most carefully examined by the Committee on Animal Diseases whose report was published some twelve years ago. The foundation of British agriculture is livestock. The cattle population of these islands is maintained by a continuous flow of hundreds of thousands of animals from the breeding areas in the wetter belt in the west, including Ireland, to the Midlands and to the dry cereal belt extending from Nairnshire to Norfolk, with the Devon cattle coming up into Hampshire and Sussex. No importing area of any extent could survive without this migration. Any attempt to stop it would disrupt the whole store cattle trade and with it the supply of milk and of beef. But it is possible to form closed areas in the exporting areas where the farms are small, the cattle population comparatively sparse in the mountain sheep districts, and in the county of Ayr. These would form pools of healthy cattle from which the attested herds in open areas could be recruited. The difficulties of hermetically sealing an importing area are immense, as any who has had to deal with sheep scab knows. The smuggling of cattle from Eire into Ulster during the war is a further instance of the hopelessness of the task.

I am not surprised at a considerably higher incidence of bovine tuberculosis in rural areas as compared with urban. Much of the milk in the former is peddled round the villages and scattered cottages by small producer-retailers. The bigger producer-retailers with well-established businesses founded on a hard-won reputation sell some of the best milk put on the market, but not so these little rural men. They buy all the cheap "screw" cattle in the markets, their premises are often badly constructed and dirty, and their methods bad. They are seldom, if ever, visited by the sanitary authorities and their milk analysed, and they escape all the controls to which the farmer selling to the wholesale buyer has to submit.

Attested herds alone, closed areas alone, will not eradicate tuberculosis entirely, but both methods pushed forward vigorously, with better prices for the better milk, will in conjunction go a long way to achieve success.

Mr. J. W. Salter Chalker: Speaking as Chairman of the Diseases of Animals Committee of the National Farmers' Union I would like to say that the farming community view very seriously the subject under discussion. They are not only concerned because of the part bovine tuberculosis plays in the general economy of animal husbandry but are particularly anxious that the milk supply in every way and particularly in this respect should enjoy the confidence of the public and the medical profession.

The problem as indicated by Professor Dalling and Mr. Ritchie is a very large one. It is not a responsibility which the agriculturist should be expected to shoulder on his own. It is unfortunate and very unfair that so often when the question is referred to in the Press it should be expressed in terms reflecting unfavourably on the farmer.

Farmer pioneers who sought to eradicate tuberculosis from their herds before the Ministry's Attested Herds Scheme was introduced received only meagre compensation for their public-spirited action; they received no real measure of support from the Ministry, the dairyman or the consumer, in so much as they only received a premium on the very small proportion of their production which was purchased by the public as T.T. milk.

The Ministry's Attested Herds Scheme was a considerable step forward and it was unfortunate that at the outbreak of war it was found necessary to withdraw it. Its later reintroduction with a premium on the whole production of milk from T.T. licensed herds was indeed welcome and has meant considerable progress in numbers of attested herds. However this is as it is, the farmer to-day is not satisfied with this progress and a resolution was passed at the last meeting of my Committee requesting me to approach the President of the Union in order to seek an interview with the Minister of Agriculture as to the urgency of starting the attested free area scheme at the earliest possible moment.

Bovine tuberculosis is a national responsibility and the farming community are prepared to play their full part in its eradication.

Dr. W. M. Crofton said that the most hopeful thing that he had heard during the discussion was the fact that extensive trials were being made of preventive inoculation, which, he considered, was the only hope for the elimination of tuberculosis, both in domestic beasts and in the human population. He did not think, however, that a live antigen such as B.C.G. was the proper material to use. Live antigens for prophylaxis were not as efficient as dead antigens because live antigens were energetically precluded by the endothelial cells of the capillaries from getting to the healthy tissues of the body,

pay compensation as is done in U.S.A. and Canada. This is possible there as the incidence of tuberculosis is about one-tenth of ours, but financially impracticable here while also very wasteful. A third plan is to brand the reactor and then let loose for the owner to do what he likes with him. I see considerable drawbacks in this plan and it is a very controversial veterinary problem. The fourth procedure is the one now operative, i.e. to turn out of the herd unmarked and unsupervised. This often simply means a transference from one herd to another and is a profoundly unsatisfactory procedure.

In my Mitchell Lecture delivered in 1933 (*Brit. med. J.* (ii), 905) I suggested another method, which although it has had lip-service approval has never been put into practice. As I still consider this is the right, and indeed the only satisfactory, way to deal with the reactor I reproduce my essential points:

"The reactors with no clinical signs are mostly in good health, giving normal milk, and are not excreting tubercle bacilli or only very occasionally. There is considerable evidence that the majority of these animals, if placed under good conditions, show little or no progressive tuberculosis, and will for long periods yield normal milk free from tubercle bacilli. If their milk can be safeguarded, and if they can be prevented from infecting other cows, why slaughter such valuable animals? The scientific method is to keep the reactors together upon separate farms containing nothing but reactors. Periodical veterinary inspection would weed out any becoming clinical cases, and the cows would have to be kept (as all cows should be) under good open-air conditions. I see no objection to their milk being sold for human food in the open market, after being subjected to efficient pasteurization. Regular bacteriological tests, before and after pasteurization, would soon demonstrate the validity as regards the safety factor of any such scheme. The cows would produce calves in the ordinary way, and if the calves were brought up on Bang's principles and segregated in their own buildings and fed on heated milk they would grow up non-reactors, and would serve as that very necessary thing—a storehouse of non-reacting cows to complete the herds of non-tuberculous cows depleted by the removal of reactors.

"The price paid to an owner for the reacting animal should be the price of a damaged cow, since obviously a cow infected with tuberculosis is not worth the price of a healthy cow. The exact figure is a matter for discussion, but as a basis of argument it might be called a two-thirds value, thus making the owner lose something like his share under the United States of America scheme. It may be suggested that such a herd of reactors with veterinary inspections, bacteriological tests, and pasteurization would necessitate milk charges above the normal economic price. The bacteriological testing should be done free by the County Public Health Authorities as their share, while they would naturally supervise the pasteurization. In view of the fact that the herd only costs two-thirds of one of healthy animals. I believe the milk could be produced at current rates. The herds would naturally be of considerable size.

"Under my proposals, instead of numerous herds made up of a mixture of reactors, and non-reactors as at present, there should be herds in which the cows were non-reactors and herds in which they were all reactors".

Every veterinary surgeon knows how rapidly tuberculosis will spread from an infected animal introduced into a tuberculosis-free herd, and separate herds seem simple common sense.

In actual fact we get this sort of thing now but under the worst possible conditions. A producer of "Accredited" milk lured by the higher bonus for "T.T." milk has his herd tested, and finds a large proportion are reactors. He removes the non-reactors to new premises and starts them as a T.T. herd. He leaves the reactors in his existing herd and continues to sell the milk from these cows, all of which are tuberculous, as *Accredited* milk and to sell it *raw*. This is perfectly legal and I have had officially to pass many such cases. The division into two herds is as I suggest, but instead of the reactor herd milk being pasteurized and the animals rigidly supervised it is sold *raw* and as a superior quality milk under the designation "Accredited".

I suggest that the provision of herds free from tuberculosis would be greatly speeded up if my solution for the reactor problem was adopted in practice. Given the necessary legal power I cannot visualize any serious practical difficulties.

Section of Dermatology

President—SYDNEY THOMSON, M.D.

[December 20, 1945]

Pityriasis Rubra Pilaris with Ainhum and Syringomyelia.—K. TATZ, M.R.C.S., L.R.C.P.
(for H. W. BARBER, M.B.).

R. G., aged 51 years. Family and personal history uneventful until 1917 when he developed keratoderma of the palms and soles. About two years later, there developed a scaly rash on his arms and legs which was diagnosed as psoriasis at the time. At about the same time, there developed ainhum-like constrictions and deep painful fissures on his palms and fingers. Six years ago a fissure at the base of his left thumb deepened to such an extent that the thumb fell off; this was not accompanied by any pain. During the next five years the remaining four fingers of the left hand were lost.

In 1944 he had difficulty in moving his left shoulder. X-ray revealed a Charcot joint and a diagnosis of syringomyelia was made.

On examination the patient shows marked keratoderma of the palms and soles. The thumb and distal halves of the fingers of the left hand are missing. All the fingers of the right hand have deep ainhum-like constrictions encircling them. On the forearms, legs and knees there are patchy, scaly psoriasiform areas. On the back of the wrist and fingers there is some follicular hyperkeratosis. The face and scalp are not involved.

Neurological examination reveals typical signs of syringomyelia.

Plasma protein and hippuric acid tests normal.

Blood carotene and blood vitamin A normal.

Biopsy from the back of the hand showed changes compatible with pityriasis rubra pilaris.

Comment.—This is a case of a man who developed keratoderma and fissures with ainhum-like constrictions and a psoriasiform lesion twenty years before the development of syringomyelia with subsequent loss of the fingers of one hand.

The question arises whether all the skin changes are due to syringomyelia or due to pityriasis rubra pilaris, or some allied condition complicated by the syringomyelia. The changes in the hands preceded the syringomyelia by many years; this together with the presence of lesions on the lower limbs where there are no sensory changes is, I think, in favour of it not being due to syringomyelia. Or is this case similar to the case shown by Dr. Wigley in 1929. Hyde (1910) records three similar cases and Stelwagen (1902) records a similar case complicated by generalized pityriasis rubra pilaris. In none of the recorded cases was there any note made of nervous changes except Drummond's case (1939) where he states there were no nerve changes. Hyde in his chapter on ainhum states:

while dead antigens were freely admitted and produced a vigorous response by the manufacture of specific antibodies.

Complete protection against assaulting doses had been produced by him experimentally at University College in Dublin in both guinea-pigs and rabbits with a human type tubercle bacillus solution, all the animals surviving after a subcutaneous dose of both human-type and bovine-type tubercle bacillus. Therapeutic trials in the field in France and in South America in animals were 100% effective. A similar prevention in human beings had been produced by him in practice in Ireland in members of tuberculous families, and a trial producing 100% survival of infants born of tuberculous mothers had been reported by Dr. Eric Pritchard from the Vincent Square Infants' Hospital twenty years ago. He could not understand why the medical and veterinary profession so obstinately refused to have anything to do with this antigen and this demonstratedly successful method.

Mr. John Francis said that it had been estimated several years ago that 40% of dairy cows were tuberculous, and in some areas this was no doubt correct; unfortunately many people had come to believe that 40% of all cattle were tuberculous. As Mr. Ritchie had pointed out this was very far from the truth.

It could not be too strongly emphasized that the main spread of infection occurred in the cowshed and that probably 90% of all cattle were infected by the aerogenous route. There was much less danger of infection when cattle were at pasture.

Efforts to reduce the incidence of the disease by attempting to detect "open cases" would not have been made if there had been a proper understanding of the pathogenesis of the disease. He doubted whether B.C.G. would be of any great assistance in the fight against tuberculosis. M'Fadyean had said that there was really only one method of establishing a tubercle-free herd and that was by the application of the tuberculin test and the elimination of reactors. The method had been applied on an area basis in the U.S.A., Finland, Guernsey and Norway, and in each country the disease had been practically eradicated; good progress had been made in Canada, and even in Denmark where the incidence was high. In Great Britain the Attested Herds Scheme was begun in 1935 and to-day there were now nearly a million cattle in officially tubercle-free herds, but further real progress would probably depend on the establishment of tubercle-free areas.

Salmon, the first Chief of the Bureau of Animal Industry, U.S.A., wrote in 1906: "When public sentiment favours the eradication of tuberculosis in animals the task will not be found an impossible one." The statement was based on a very careful appraisal of the knowledge then available but must have been partly a declaration of faith. The incidence of bovine tuberculosis is high in Great Britain, but to-day there is much evidence that when public opinion is favourable we can confidently begin the process of "stamping-out" bovine tuberculosis.

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"Some cases of anhidrosis are associated with trophic sensory and vasomotor changes particularly in the limb where the anhidrosis is occurring; the skin of the part may be scaling with wasted muscles, absence of tendon reflexes, and sensibility decreased; keratoderma may be conspicuous." Could not this picture that Hyde describes be similar to this case?

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Dr. H. W. Barber: Before I say anything on this case I should like Dr. Leitner, who has been investigating pityriasis rubra pilaris for some time past, to speak to us.

Dr. Z. A. Leitner (*Abstract*): Recently, through the kindness of Dr. Barber, we had the opportunity of studying a family affected by pityriasis rubra pilaris. Two members were under continuous observation for over twenty-two months and in addition three more members of the family with the same disease were investigated (Leitner and Moore, 1946b).

Two forms of pityriasis rubra pilaris—a hereditary and an acquired one—have been repeatedly described (Touraine, 1942). In the course of our investigation we were impressed by the fact that although five of the living six siblings were affected by the disease, two of them were always considered healthy. One of these two supposedly unaffected persons was a man of 45 whose mother was suffering from the disease; his sister had a twenty-five years' history and her son a fifteen years' history of the generalized form of pityriasis rubra pilaris. [These two cases were previously demonstrated to this Section (Leitner, 1945, 1946).] His own son was free from any skin disease, the elder daughter had a very mild form, but the younger one had a more or less generalized pityriasis rubra pilaris, which was first considered as a congenital "eczema". Throughout his life the man himself had palmar hyperkeratosis with typical acuminate papules and projecting cones on the wrists, elbows, knees, and the back of the proximal phalanges, and although he was in the Army for over twenty years, his condition was never diagnosed.

This family history stimulated us to study the hereditary aspects of the disease. A survey of the literature since the beginning of the century yielded 14 more unquestionable instances of familial occurrence of pityriasis rubra pilaris. The data of these 15 families were submitted to Dr. E. B. Ford who agreed that the details of their histories were consistent with the view that pityriasis rubra pilaris is an inherited disease, namely a single autosomal heterozygous condition without sex linkage.

Another aspect investigated was the relationship of pityriasis rubra pilaris to vitamin A metabolism. Since Pettler (1936), several authors have described it as a vitamin A deficiency disease. Some of our cases (the severely affected) had a persistently low vitamin A and carotene level in the blood but others were within the normal range. The degree of clinical involvement in our cases roughly corresponded to the decline of the vitamin A level.

Several other factors also suggested a disturbance of vitamin A metabolism. The rise in the blood vitamin A level after a massive dose of vitamin A usually reaches its maximum after five to eight hours (Leitner and Moore, 1946a). In pityriasis rubra pilaris this was often delayed and to achieve this in one case it took more than two months of continuous dosing. We do not suggest of course that pityriasis rubra pilaris is simply a vitamin A deficiency disease; it may, however, be pertinent to refer in this connexion to rickets resistant to vitamin D treatment first described by Albright (Albright *et al.*, 1937). In his cases normal doses of vitamin D were without any effect, but the disorder of metabolism was corrected by giving continuous enormous doses for a long time (up to 100 times the normal therapeutic dose). After stopping the excessive vitamin D medication florid rickets reappeared within a few weeks' time.

During vitamin A treatment (up to 250,000 i.u. daily for many months) the skin condition improved considerably in all our cases. Perhaps it may be of some importance to mention that every deterioration of the skin condition during vitamin A treatment coincided with a sharp fall in the blood vitamin A level. It cannot yet be stated with certainty whether this coincidence was due to an interference with the absorption of vitamin A, or with its impaired storage or release. As the liver is the main storage organ for vitamin A it is open to speculation whether and how the disturbance in vitamin A

metabolism may be related to this organ. In our cases various liver function tests were carried out and revealed gross impairment of liver function.

Moreover definite signs of endocrine disturbances were also present in our cases indicating a pituitary involvement (cyclic deterioration of the skin condition before menstruation; regular generalized spread all over the body with erythrodermia during pregnancies; cryptorchism).

If we are correct in suggesting that pityriasis rubra pilaris is always an inherited condition, the case of Dr. Barber and Dr. Tatz showing pityriasis rubra pilaris and syringomyelia is of great importance, as syringomyelia is often considered as a congenital disease. Therefore in Dr. Barber's patient two different systems of ectodermal origin appear to be affected, a combination which does not seem to have been described before.

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Dr. H. W. Barber: A question has been raised as to whether this man has pityriasis rubra pilaris at all. I did not think there was any doubt of it when I first saw him. On examining him carefully the typical follicular papules can be seen. I agree that the lesions on the legs are like psoriasis, but in my experience when one sees an early case of pityriasis rubra pilaris, it is often impossible to distinguish it clinically from psoriasis. In the former disease, however, an erythrodermia of the palms and soles soon develops, as a rule, and later the characteristic follicular papules. As will be seen from the section submitted in this case, the histological picture is unlike that of psoriasis. The chief interest is the association with syringomyelia and the ainhum-like condition of the fingers and toes. In Dr. Wigley's case the latter was accompanied by keratoderma of the palms and soles, which may, perhaps, have been pityriasis rubra pilaris.

Dr. J. E. M. Wigley: I have not seen the case just mentioned since 1929 in which year I published it, so I have nothing to add.

Dr. F. Parkes Weber: When I was in Paris while Charcot was teaching, this kind of condition—not the dermatological part of it, but the neurological part—was very much talked about, and it was then called "Morvan's disease". After much discussion Morvan's disease was gradually acknowledged to be not a peculiar mild form of leprosy but a clinical type of syringomyelia—the so-called "Morvan type of syringomyelia". The extremely exaggerated knee-jerks and the history of diminished sense of pain and heat in the upper limbs confirm this diagnosis in the present case. I should not be surprised if the callosities were not likewise due to the syringomyelia. Anyhow, in this particular case, the ainhum-like lesions must be part of the syringomyelia. Spontaneous dropping off of distal segments of fingers or toes, as in this man, would in the Middle Ages have branded the patient as a leper.

Lupus Vulgaris treated with Calciferol.—G. B. DOWLING, M.D., E. W. PROSSER THOMAS, M.D., and H. J. WALLACE, M.D.

CASE I.—Mrs. Edith G., aged 73. Lupus of the superficially ulcerative and crusting type began ten years ago on the nose and gradually spread across the cheeks. She has been under the care of the Skin Department at St. Thomas's Hospital during the whole of the period. She was unable to tolerate general light treatment and until October 1943 she was treated by local measures chiefly. Though controlled to some extent, the gradual progress of the disease was not checked by these measures. In October 1943 she was given calciferol, without further local treatment, 50,000 i.u. twice daily, continuing on this dose until July 1944, when she was evacuated to the country. From that time she had no further treatment. She returned to London in October 1945, when as far as could be seen the lupus had disappeared altogether.

CASE II.—Mrs. Alice M., aged 54. She was first seen on January 18, 1945, with extensive lupus of the left side of the face and neck and of the left forearm and hand. The lesions on the forearm and hand were severely ulcerated.

She was given calciferol, 50,000 i.u. three times a day and returned on February 8 with all lesions showing good response. The dose was then reduced to 50,000 i.u. twice daily.

By March 8 the forearm and hand were healed and the lupus on the face and neck was also regressing.

Her state to-day is most satisfactory. All lesions are completely healed and her lupus is clinically cured.

CASE III.—Miss W., aged 35. Patch of lupus on right side of face since the age of 3. Has had most of the usual forms of treatment including Finsen light. Marked activity of the lupus, particularly under the chin, when first seen three months ago. No evidence of tuberculosis elsewhere. Has been treated exclusively with calciferol by mouth, 100,000 i.u. daily, with great improvement.

CASE IV.—Mr. H. E., aged 53. First came under observation twelve months ago with warty lupus of the left buttock. This had first appeared some seven years previously and had been gradually spreading. No evidence of tuberculosis elsewhere. Treatment was begun with one painting of acid nitrate of mercury together with daily administration of 100,000 i.u. calciferol by mouth. Improvement was immediate, out of all proportion to the effects of one application of acid nitrate of mercury. Treatment subsequently was continued with calciferol only, in the same dosage. There has been no evidence of activity for the past two months.

CASE V.—Albert E., aged 34, who for many years before had suffered from tuberculosis of the spine and right hip, developed in 1937 warty lupus of the left thenar eminence. For this he was treated first in 1938 at St. Thomas's Hospital. He then moved elsewhere but returned in June 1945 with an additional warty lupus on the inner aspect of the left foot, which had begun two years previously. Meanwhile, the original lesion had spread serpiginously over the palm and on to the back of the hand between the thumb and forefinger. Under calciferol, 100,000 i.u. daily, the lesions in both areas have completely cleared.

Dr. G. B. Dowling: I do not think any of these cases call for discussion in detail. One of them (Case I) is interesting because she has remained free from lupus though she stopped taking calciferol eighteen months ago. Three of the others (Cases II, IV and V) are remarkable for the rapidity of cure; improvement in each especially in Case II, which was severely ulcerated, took place within a few weeks, and they are all now completely cured. Case III, the lupus of the right cheek and submandibular region, is showing what I consider to be an average response to treatment. She has been taking 100,000 i.u. of calciferol daily for about three months, during which the greater part of the lupus has disappeared though some nodules remain in one area. She will probably require treatment for a further three months, or perhaps rather longer.

These five cases, together with the six who were presented to the Section on November 15, and a considerable number of others which have responded in a similar way to the same treatment, can leave no room for doubt that calciferol in adequate dosage will cure a substantial proportion of cases of lupus. The question that must interest us now is, how does it act? I do not think there is anything to be gained by making guesses; it will be better to try and enlist the interest of those who are best qualified and equipped to set about such a problem. In that case we and others who have charge of clinical material should be able to co-operate in the work of investigation.

Dr. J. E. M. Wigley: May I mention a case which I saw shortly before the previous demonstration? This was a girl aged 3 who, five months after measles, developed multiple disseminated lupus on arms, legs, and face. After the last demonstration (November 15) I put her on calciferol, about 15,000 units twice a day. A fortnight later each of the lupus nodules had become rather indefinite in outline, with a little erythematous halo around it, and one could say optimistically that they all showed signs of disappearing.

Another case was one of a florid, tumid lupus in a woman. Within three weeks of taking 150,000 units of calciferol a day the tumidity had disappeared and the nodules showed signs of flattening.

Lieut.-Colonel F. F. Hellier: It would now appear that we have constructed our wonderful light equipment, our Kromayer, our Finsen-Reyn lamps, merely for the sake of applying a dose of calciferol to the skin, when it could have been given more readily by the mouth. I am particularly interested in the fact that the French discovered the same thing at about the same time. I asked Dr. Dowling if he knew of the French work, but the two were quite independent. The French method, called the method of Charpy, is described in the *Annales de Dermatologie*, for July 1945. The following results were obtained with vitamin D: lupus vulgaris, 20 cases, 20 cures; vegetating tuberculosis, 1 case, 1 cure; lupus erythematosus, 5 cases, no cure, &c. The writer does not give any reference to Charpy's original paper. I feel that this is a fundamental discovery.

Dr. W. J. O'Donovan: Our congratulations are due to Dr. Dowling and his colleagues on all these cases. In a previous discussion on lupus those of us who have devoted years to the subject had to undergo a minor castigation on the ground that we had made a "fetish" of light treatment—an unpleasant word to be published regarding the work of one's colleagues. But Dr. Dowling will find that there is no fetishism of obstruction. There will certainly be none in our lupus clinic at the London Hospital. There is a great institute in Rome which affects to cure lupus by the giving of medicine; it is not run by the profession and it has the highest testimonials from people of eminence outside our profession. A similar claim is made in advertisements from the North of Scotland, I believe, for a certain medical cure of tuberculosis by a lime solution made from calcined bones. I do not wish to advertise it. It may be, as has happened before in medical history, that in fact a serious attack has been made on the disease by those outside our ranks and we are now seeing its adoption and perfecting.

Dr. Franklin Bicknell: There has been very little work done in England on the toxicity of calciferol; it would be of value and easy, now that large doses are being given, to check unconfirmed reports about the premonitory symptoms of poisoning—such as acute tenderness of the back of the head. Presumably some cases of lupus have vascular degeneration, coronary disease or nephritis; in all these conditions calciferol is especially dangerous, so it is important to determine the minimum dose which is effective in curing lupus. It might be possible to give calciferol in an ointment, thereby securing a higher concentration in the lesion and a less high concentration in the arteries.

Kaposi's Idiopathic Sarcoma (With sections).—J. E. M. WIGLEY, M.B.

C. C., female, aged 43, a native of Devonshire. First seen in June 1945 for a painful lesion on the ball of the left foot which had been present about five to six months. The patient stated she had had two previous lesions which had healed with simple local treatment only.

When first seen the lesion was a red, semi-solid angiomatous-looking tumour about the size of a filbert nut which was flush with the surface of the sole of the foot. There was no epidermis over it. A provisional diagnosis of granuloma pyogenicum was made and the tumour removed by diathermy. The removal was not, however, very complete, and the tumour re-formed. In July the whole lesion was excised and sent for section. The surgeon making the excision said that he found the tumour unexpectedly tough.

The section was reported on by the pathologist as a hæmangio-endothelioma and quite definitely not a melanoma.

Subsequently it has been treated with several exposures by penetrating X-rays with only moderate benefit.

When seen on November 22 there was a very definite margined bluish erythema along the inner side of the sole of the foot and also spreading a few inches up the leg. The erythematous area felt slightly indurated. This appearance supported a suspicion that the lesion might be Kaposi's idiopathic sarcoma, which I had begun to consider.

I then examined the section again carefully, and the considerable vascularity and cellular infiltration (rather aggregated around the new vessels) seemed to me to support the clinical suggestion.

Further staining of another section for iron pigment showed a moderate amount of this to be present and seems to me sufficient to justify the diagnosis.

Dr. F. Parkes Weber: There is no Jewish ancestry in this case, and the patient is a woman, not a man. The majority of cases of multiple hæmorrhagic sarcoma in this country—in London at all events—are, and have been for a long time, male cases and of central European Jewish origin. I only mention this to point out that in this case one ought to be particularly careful to confirm the diagnosis considering the patient's sex and ancestry. To my mind, moreover, the case does not look like a genuine one of multiple hæmorrhagic sarcoma. The history of the chronic sore following the growth on the sole suggests to me that the growth was a typical pyogenic telangiectatic granuloma—what the French call "human botryomycoma". I cannot explain the recurrent telangiectatic borderline on one side of the foot, but I suspect that it has something to do with the ulcer on the sole. If that ulcer were healed properly, I think that all the signs of hæmorrhagic sarcoma would disappear.

Dr. Walter Freudenthal: I agree with Dr. Wigley's diagnosis. This form of Kaposi's disease is rare and can easily be missed. A good illustration of it is found in *Jadassohn's Handbuch*, vol. 12/3/2, p. 913.

Dr. J. E. M. Wigley: Recent figures do not appear to support the marked preponderance of Kaposi's sarcoma in the Jewish race, though they do indicate that most of the patients

are of the male sex. The other point is that in this case the original tumour was not soft. The surgeon who tried to remove it remarked to me that it was unusually leathery, which does not suggest to my mind botryomycosis hominis.

Black Hairy Tongue.—C. H. WHITTLE, M.D.

C. R., a man aged 32. Post Office worker. Six months' history. He smokes thirteen cigarettes a day, and gets some post-nasal catarrh. General health good.

The tongue shows long brownish-black hairs on its posterior third, rather more pronounced on the right than on the left.

Microscopy shows the "hairs" to be composed of horny cells, many with nuclei, but showing degenerative changes, in some of which masses of yeast-like bodies are arranged in mosaic form.

Cultures: Monilia in abundance. (Cultures shown.)

Only some of the "hairs" show fungus, but the amount of yeast-like bodies in these is very striking indeed. I had no difficulty in growing the fungus. I should welcome any suggestions as to treatment.

Dr. G. B. Dowling: The mosaic-like arrangement of the spores in the hairs is very striking, and seems to me to suggest strongly that their presence can hardly be purely adventitious.

Dr. W. N. Goldsmith: In 1928 (*Brit. J. Derm.*, 40, 366) I showed at this Section a case of chronic superficial glossitis, with black fur, which had been carefully studied bacteriologically by Dr. R. Ralph. On two occasions he obtained from it in pure culture the two organisms *Nocardia lingualis* and *Cryptococcus lingua pilosa*, which were described. Ralph thought that these two organisms represented a true symbiosis. He had found them together in three other cases of black hairy tongue and had not met them in any other condition. I had another case, however, unaccompanied by glossitis, from which no unusual organisms were cultured. The most effective treatment was massaging the tongue with Monsol ointment.

Lupus Erythematosus in a Girl aged 10.—C. H. WHITTLE, M.D.

J. B., aged 10. A two years' history of an eruption on the nose, cheeks, and scalp, in bat's-wing distribution on the nose and cheeks. The lesions are bluish-red with tough adherent scales and there are several outlying plaques on the face. On the scalp there are two or three areas with similar infiltrated plaques with some hair loss.

The child appears in fair health otherwise, but is liable to sore throats.

The factors which favoured the diagnosis of psoriasis were the good response to sunlight and the presence of undoubted psoriasis in the mother in the usual places, namely knees and elbows. But I am afraid this will prove to be lupus erythematosus. The whole picture with the adherent scales is fairly typical, and I am hoping we shall find a focus. The tonsils are a possible focus, but we shall have to consider the lungs as well.

POSTSCRIPT (9.1.46).—X-ray of chest—no abnormality. Mantoux 1 : 1,000, human and bovine, negative. E.N.T. examination, negative. X-ray of sinuses—left antrum shows slight infective changes.—C. H. W.

P.P.S. (9.3.46).—X-ray of chest negative. Calciferol 30,000 units daily by mouth for two months has been accompanied by some improvement.—C. H. W.

Dr. H. W. Barber: The eruption in this case is clearly lupus erythematosus. Apart from the patches on the face and scalp, she has typical lesions on the lobes of the ears. I think that this form of lupus erythematosus, in which the patches are rather indurated, and in which there is very marked hyperkeratosis with the production of thick adherent scales, is usually of tuberculous origin.

Dr. G. B. Dowling: I understood Dr. Whittle to say that he thought of trying calciferol in this case. I have already treated several cases of lupus erythematosus with calciferol in large doses, including one with an associated tuberculous adenitis, histologically confirmed as tuberculous. In this case as in others calciferol had no effect though the adenitis appeared to be regressing. In a case of sarcoidosis under the care of Dr. Wallace, calciferol has proved equally ineffective.

Dr. W. J. O'Donovan: These are cases in which the distinction between lupus erythematosus and lupus vulgaris appears very inscrutable. I have experience of a very few cases in which over the course of years of observation the diagnosis in very skilled hands has varied at intervals from the one to the other. This may explain unexpected results in treatment.

Dr. W. N. Goldsmith: The face, as a rule, gets worse in the summer, and the fingers better.

Dr. G. B. Dowling: The lesions to which Dr. Goldsmith refers are, I imagine, of the Hutchinson's chilblain lupus type, in which circulatory hypostasis is the predominant factor.

Dr. Whittle: I have never before seen lupus erythematosus in a child so young.

Dr. W. J. O'Donovan: I have seen lupus erythematosus twice in children as young as that, and they died rather speedily. Someone on seeing this case mentioned penicillin. I have three complete cures of lupus erythematosus, of two years' standing or more, with penicillin. I do not think that penicillin will be claimed as a cure for a case with a primary tuberculous focus.

Dr. Barber: Of what did the young children die?

Dr. O'Donovan: In one of the cases the post-mortem showed nothing but cloudy swelling, no tuberculosis and no discoverable focus of sepsis; the other was a private case, and it was not pursued to the end of the story.

Dr. H. W. Barber: In 1943 I described in a letter to the *British Medical Journal* (May 8 (i), 580) a remarkable case of a child, aged 7, who had apparently had lupus erythematosus since infancy. When I saw her, the eruption was very extensive, involving the bat's-wing area of the face, the scalp, neck, ears, back and arms. As in the case under discussion, it was of the indolent hypertrophic type, with thick adherent scales and marked follicular hyperkeratosis. The child had already had one operation for tuberculous cervical adenitis with abscess formation. After the operation the eruption completely disappeared, although she lay out of doors in the sun to which she had formerly always been sensitive. It relapsed, however, with the appearance of tuberculous adenitis around the operation-scar and under the chin, and became more extensive. Another operation was performed, and the eruption improved greatly, but later abdominal tuberculosis supervened when she was under Dr. Mumford's care, and she eventually died of general tuberculosis. If one considers the following points one must, I think, logically conclude that in this case the lupus erythematosus was a toxibuberculide: (1) The rarity of lupus erythematosus in young children, and the unusual severity and extent of the tuberculous adenitis; (2) the complete, but temporary disappearance of the eruption after the first operation on what was at that time presumably the main and primary focus of infection in the glands on the right side of the neck, although the child was freely exposed to sunlight which previously had always provoked an outbreak; (3) the relapse of the eruption associated with involvement of other glands on both sides of the neck and in the submental region; (4) the striking and more lasting improvement in the eruption after the second and more extensive operation; (5) the fact that the eruption, although widespread, was not of the kind usually seen in the disseminate form of the disease, many cases of which have a severe and often fatal streptococcal septicæmia.

Dr. W. N. Goldsmith: I also had a fatal case of lupus erythematosus in a young girl a few years ago. She never had any evidence of tuberculosis. She had had sore throats and occasionally joint symptoms of a rheumatic type, and she died with the usual toxic symptoms and swinging temperature. We did blood cultures repeatedly almost up to the hour of death, and they were all negative. The necropsy showed no trace of tuberculosis or of sepsis anywhere. There were a few little vegetations on the heart valves.

Multiple Keloids following Varicella.—E. W. PROSSER THOMAS, M.D.

Evelyn H., aged 14. She is said to have had a severe attack of chicken-pox six months ago, contracted from her sister, who had an average, mild attack. Many of the lesions became pustular and healed leaving numerous hypertrophic and keloidal scars. These are fairly profusely distributed over the front and sides of the neck and the upper part of the chest, and there are a few scattered elsewhere on the trunk and limbs. The lesions are showing no signs of spontaneous regression, except that they may be paling a little. There was no previous tendency to keloid formation, and there has been none subsequently. I am proposing to treat some of the more conspicuous lesions, e.g. those on the neck and upper part of chest, with Chaoul therapy.

Dr. F. Parkes Weber: This case reminds one of the rather less uncommon development of keloids at the site of vaccination. A long while ago I saw typical post-vaccination

keloids in a girl of about this age, which finally yielded to X-ray treatment. I have seen the patient since, and she has not manifested any special tendency to keloids elsewhere. I presume the X-ray treatment which Dr. Prosser Thomas advocates makes the keloids become pale and gradually causes their atrophy. The natural history of keloids, e.g. those resulting from burns, is that, however long they last, ultimately without special treatment they become pale and gradually atrophy. That ultimate atrophic process, by the way, is part of the natural history of many surgical scars: when old age is reached, sooner or later, they tend to atrophy. Unfortunately this atrophic process in old age is not altogether without its disadvantages, for instance, in regard to the yielding of scars from abdominal and rectal operations.

Dr. W. N. Goldsmith: Thorium X might prove adequate and more convenient than X-rays. It seems strange that thorium X with its slight penetration should have this consequence, but it appears, nevertheless, to do so.

The President: I suggest that the case might be left alone for a year, for I have seen conditions of this kind disappear spontaneously within a year or eighteen months.

Xanthoma of Hands.—CLARA M. WARREN, M.R.C.S., L.R.C.P.

Mrs. S. L., aged 57, has worked for three years trimming rubber. For six months she has noticed oval yellow nodules and yellow staining in the creases of the palms of the hands and of the fingers. There is a cluster of typical xanthomata on each elbow, but none elsewhere.

The patient has not got diabetes, but she comes of a family who are known to be "liverish", who have bilious attacks, and suffer from gall-bladder dyspepsia.

Blood cholesterol 340 mg. % (normal 100-120 mg. %).

Herpes Zoster.—Dr. J. JAWORSKI (introduced by Dr. R. T. BRAIN).

Dr. Jaworski described a method of treating zoster by injections of the patient's own blood. He takes 10 c.c. of blood from a cubital vein in the usual way and injects 5 c.c. under the lesions themselves in several insertions; the other 5 c.c. are injected under the skin near the corresponding spinal ganglions. In most cases one treatment only was given, but in others the injections were repeated once or twice with a day's interval. Dr. Jaworski said he had treated 31 cases of zoster by this method with symptomatic relief and early resolution of the lesions.

No drugs were administered during the treatment.

Section of Surgery

President:—ERNEST FINCH, M.D., M.S., F.R.C.S.

[December 5, 1945]

Sense and Sensibility in the Treatment of Cancer

PRESIDENT'S ADDRESS

By ERNEST FINCH, M.D., M.S., F.R.C.S.

It was almost unnoticed by the medical profession that on March 29, 1939, The Cancer Act was passed by Parliament. This was described in the preamble as: "An Act to make further provision for the treatment of Cancer, to authorize the Minister of Health to lend money to the National Radium Trust, to prohibit certain advertisements relating to Cancer and for purposes connected with the matters aforesaid."

Thus another great scourge of humanity became a statutory disease, having been preceded by tuberculosis and venereal disease. With the exception of cardiovascular diseases, cancer is the most frequent cause of death in this country, the Dominions and United States of America.

In the Bradshaw Lecture given by Sir Alfred Webb-Johnson in November 1940, which was entitled "Pride and Prejudice in the Treatment of Cancer", an attempt was made to steer a course for treatment most advantageous to the patient between the *pride* of the surgeon and the *prejudice* of the radiologist and vice versa.

The treatment of cancer was considered as a radio-surgical problem. It is, however, becoming more than that: as the influence of hormones on malignant growth, both as a causative and therapeutic factor, becomes more understood, endocrinology will play a more and more important part in the treatment. It is perhaps the arbitrary clinical division of cancer into various stages of the disease which has led to the *pride* of the radiologist and the *prejudice* of the surgeon. This clinical division has led to the realization that the treatment of each individual case should be carried out on a consultative basis and assessed by the surgeon, radiotherapist, physician and pathologist with the biochemist and biophysicist in the background.

It is by this and this alone that it can be hoped to achieve what in grateful acknowledgment of Sir Alfred Webb-Johnson's happily chosen title might be called *Sense and Sensibility* in the treatment of cancer.

It is generally admitted that about half the patients suffering from cancer need some form of radiotherapy, which can only be undertaken satisfactorily in special centres, and, in addition, intensive research must be pursued in every aspect of the cancer problem. It was in order to attain this that the Cancer Act was conceived and delivered. It must now be implemented. The responsibility is placed on the local authorities.

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when sent for found to be malignant, yet such a case was kept waiting so that obvious cases of malignant disease might be admitted first.

The treatment of the cancer patient does not end with the successful operation. The Act opens up the whole problem of the treatment of the chronic sick, many of whom are suffering from cancer.

It is necessary that beds be provided for them either in hospitals, hostels, or accommodation in "alms-houses" with adequate nursing and medical attendance.

Also patients in the later stages of the disease should have all the alleviation which modern treatment can afford.

This may mean the surgical relief of pain by operation on nerves, the spinal cord, or amputation.

Centralization of treatment seems to be necessary for the following reasons:

- (1) To secure early diagnosis.
- (2) To secure adequate first treatment. The advantage of early diagnosis is lost if the first treatment is inadequate, so it should be carried out on a consultative basis.
- (3) Radiotherapy apparatus is very expensive and mainly immobile. When such apparatus is installed it must be worked to its fullest capacity. The number of patients must be sufficient to prevent waste.
- (4) The records at a centre can be kept properly and analysed by those skilled in dealing with statistics. Moreover all cases must be recorded, whether treated or not. No one individual has had experience in dealing with a sufficient number of cases to formulate any definite opinions. A retiring surgeon has only dealt with a few hundred at the very outside.
- (5) Discussion and assessment of results at a centre would lead to clinical research quite apart from the purely scientific research of biophysicists and biochemists.
- (6) A staff of expert radiotherapy technicians would be attached to a centre, and would be always increasing their experience by dealing with the special technical difficulties of a whole region.

At the end of the last century radium was discovered and radiotherapy established. In 1929 the National Radium Commission was instituted to control the use of the radium bought as a thankoffering for the recovery of King George V.

The Cancer Act is the logical conclusion of all the research which has taken place into the sensitivity of tissues to radio-activity. The process by which a cancerous change is brought about in tissues must continue to be studied as a necessary prelude to the further means of treatment and prevention of cancer.

Prevention is a public health problem, and will become more so but, as cancer is not notifiable, the incidence of the disease can only be estimated.

The problem for the public health authorities now is not only the prevention but the treatment and also the after-care of the incurables. The education of the community should also be their responsibility. What then should be the "lay-out" for a regional organization? Any scheme must provide for diagnosis, and adequate treatment by any and all means, and it must be such as not only to deal with the primary growth but all subsequent complications.

Radiotherapy will be concentrated in comparatively few centres: regional (university) and co-operating.

The surgery can be done at more scattered centres but under the criticism of the centre and on a consultative basis. Such centres must be adequately equipped and staffed, hence recognition of hospitals rather than surgeons must be the rule. The anomalous position will arise that a surgeon is recognized as competent to deal with cancer cases at one hospital but not at another, such as a cottage or local hospital.

The surgical treatment should be carried out on a consultative basis with the radio-therapist and pathologist.

It may be that a surgical operation is necessary to determine whether a *possible* or *probable* cancer is a *proved* one.

The Cancer Act provides not only for the diagnosis and treatment of the proved case of cancer but also for those patients who are suspected of suffering from it, until the condition is proved innocent. This implies the highest histological skill of the pathologists and in order to establish a diagnosis all the resources of a large polyclinic may be necessary. The importance of a correct diagnosis is not only for the patient but for those administering the financial aspect of the Act.

A regional and co-operating centre should cater for a population of between two and

It is obvious that neither the methods of treatment at present available nor the knowledge already accumulated is being used to the best advantage. The number of deaths from cancer is steadily increasing despite the fact that the "cures" are also increasing.

The main factors contributing to the failure are:

(1) Early diagnosis is not attained. In many instances the general practitioner can make a diagnosis of cancer with great certainty, in other cases it needs the opinion of a specialist reinforced by radiological and pathological examination before a *possible* case of cancer becomes a *probable* one. In other cases a surgical operation may be necessary before a *probable* case becomes a *proved* one. The early symptoms and signs of which the patient complains are common to malignant and innocent conditions. It follows therefore that any clinic which deals with the diagnosis of cancer (which is the declared purpose of the Act) must be equipped to diagnose non-malignant conditions. There should therefore be no *ad hoc* cancer diagnostic clinics in a hospital. The patients should pass through the ordinary out- and in-patient channels.

(2) The first treatment given is not always adequate and this is the all-important treatment. Cancer patients should therefore only receive treatment from physicians, surgeons and specialists of the required degree of training and experience, and if the type of cancer falls within an acknowledged specialty then they should be directed to the appropriate specialist, even if it entails referring them to another centre not necessarily a larger one.

(3) Sufficient use is not made of past experience. This would be rectified if the diagnosis and treatment were under a central (regional) organization with co-operating centres.

The surgery need not be done at the centre but under the criticism of the centre. Treatment should be organized on a consultative plane by regular discussion of cases and results by all concerned. In this way the "Pride and Prejudice" of those interested would be replaced by "Sense and Sensibility" to the advantage of all, especially the patient. The results of treatment could be sifted scientifically and judged dispassionately.

There is no suggestion in the Act of creating "The Cancer Surgeon," but that the treatment should be under an organization which would secure early diagnosis, adequate first treatment, and assessment of results.

How can this be attained? It must be by education both of the community and the medical profession.

Many will disagree with educating the community, thinking that thereby "cancer-dread neurasthenics" will be created. The public must know, however, that the only early sign of a cancer is change in form or function of some organ, and that it is painless in the early stages except in the case of bone. Education of the community has, however, been very successful in the United States and New Zealand. In cancer of the breast the margin between hope and despair is marked by involvement of the axillary glands, not merely clinically but microscopically. On one side of the line there is a 70% to 90% five-year cure, on the other 30% or less.

In 49% of cases the axillary lymph nodes are affected with no clinical evidence of their involvement.

The patient delays asking advice from ignorance, fear, false modesty and gullibility. The Act has provided against the last-mentioned by forbidding the advertisement of "cancer cures".

The medical profession must be educated both in the undergraduate and postgraduate training. Too much stress is laid on the differential diagnosis, and too little on the biopsy results. The arrangement of the cells is the only certain diagnostic test. The present training leads both the undergraduate and postgraduate to believe that a lump in the breast which is not fixed, with no nipple retraction and no palpable axillary glands, is innocent, whereas a biopsy would perhaps prove it to be malignant and thus save valuable time, as adequate early treatment could be given, and instead of 7,000 women dying each year from cancer, the number might be reduced to 1,000.

The general practitioner is the first line of defence, and must be an integral part of the scheme and kept informed of the work at the centre and the results achieved.

Delay in treatment is due to causes other than the delay in diagnosis. There is delay between seeing the practitioner and the surgeon, either from ignorance or fear. The distance from the hospital need no longer be a cause as the Act provides for travelling expenses for the patient and a companion, but the scarcity of beds is one of the main causes for delay. Moreover, a case may be put on the waiting list as being innocent, and

What is the purpose of an abdominal incision? What should it do and what should it not do? An incision should give access to the part to be attacked, and room for the required job to be done. It should be extensible in a direction that will allow for any reasonably probable extension of the scope of the operation. It should interfere as little as possible with the functions of the abdominal wall in the immediate post-operative phase, and it should finally leave it as strong as it was before.

When we demand access to the part to be attacked, we do not mean the most direct access to the whole field of operation, but the best access to its most difficult parts. When we demand extension, we are not asking for an incision that will cover any number of wildly wrong diagnoses, but one that will allow reasonable latitude in scope. A good incision must bring the surgeon to parts that cannot be brought to him, which usually means to roots or pedicles of organs, which again usually means the mid-line, for that is where arteries sprout and ducts empty.

The first essential of an incision in securing access is that it should be placed right. It is equally important that it should be large enough to admit the surgeon's hands and the ordinary tools of his craft. Telemanual technique is indispensable in the various specialties that might be grouped together as orificial surgery, but in the abdomen it is perverted ingenuity. Operating with long instruments and stalked lights has the dramatic appeal of a peepshow, but it can never be as safe or as gentle as work with fingers. One of the truest aphorisms in abdominal surgery is that of Fagge: "Make your incision twice as long as you think it ought to be; then you won't have to enlarge it much." The small incision is the vice of the callow, the cosmetic, and the commercial; it means at best more retraction and trauma than is really necessary, at worst a job poorly done or a necessary job left undone.

The second essential is extensibility. Before opening the abdomen at all, a surgeon must ask himself "What is the matter? What am I proposing to do? What else may I possibly be forced to do?" and he must so plan his incision that he can certainly do the necessary, and can, if need be, extend it to do the contemplated additions. But he must have some idea of what organ he proposes to attack, or at any rate in which compartment of the abdomen he is going to perform. He can extend the standard incisions, the median and paramedian and the lateral oblique or transverse, to a length of twelve inches or more without gross structural damage, but it is seldom right that he should do so. If the diagnosis was right but the operation unexpectedly difficult he needs no more than a moderate extension; if the diagnosis was wrong, he is faced with the difficult alternatives of opening the abdomen like the mouth of a yawning hippopotamus, or closing his original incision and making the right one.

The difficulty arises above all in operations for acute abdominal emergencies. An incision correctly planned for acute appendicitis can be extended to cope with an appendix that is gangrenous and fixed in some unexpected situation; but it cannot be enlarged light-heartedly to deal with a duodenal perforation, an inflamed gall-bladder, a gangrenous pancreas, or a ruptured ectopic gestation. When, after careful investigation and earnest thought, there remains a doubt about the nature of an acute abdominal catastrophe, I believe the surgeon should follow the two simple rules that enable bookmakers to live in Park Lane and spend their week-ends at Brighton: "Bet on probabilities and cut your losses." In the acute abdominal stakes, the form is—appendix odds on favourite, ten to one the field. Therefore when in doubt he should make an appendix incision. In nine cases out of ten he will be right. In the tenth he will establish the diagnosis by fluid that escapes and by gentle exploration with the finger, and can close the first incision and perform the necessary operation through the correct one, having wasted less time and done less damage than if he had started with some compromise applicable to both conditions and suitable to neither.

While the standard incisions I have mentioned can, but very seldom should, be extended to considerable lengths, others are inextensible, being limited either by anatomical confines or by the need to avoid irreparable damage. In the first category are transverse incisions much above the umbilicus which are cramped by the rapidly narrowing epigastric angle, in the second are all vertical incisions near the outer border of the rectus. No surgeon who has seen, as I have, the victim of a full-length incision in the linear semilunaris, the abdominal wall deformed by a large unilateral bulge, the umbilicus in the nipple line, will ever forget the lesson.

The third criterion of a good incision is that it should do the least harm to the abdominal wall itself, to the structures underlying it, and to the patient. In the abdominal

four million. This number is necessary to keep the radiotherapeutic centres economically busy.

There should be an autonomous efficiency and sufficiency in all intermediate and district hospitals with a smoothly working two-way traffic system so that the specialist can go to the periphery and the patients pass from the periphery to the centre.

The technique of radiotherapy will be changing much more rapidly than that of surgery.

Who should do the radium implantation?

Whoever does it must see that:

(1) The help of the radiotherapist and biophysicist is obtained to plan the position and extent of the implants.

(2) The implantation is checked by radiology and the field checked.

(3) The doses are recorded in such a way that the radiotherapist, if subsequent treatment is needed, can successfully and safely adjust the dose.

(4) There is a regular follow-up for at least ten years.

In addition to having a radiotherapeutic department established at the fully equipped regional (university) and co-operating hospitals, there must also be the closest co-operation between them and the district hospitals where the surgery can be done.

There must be consultative centres scattered over the whole region where the general practitioner can send his patients at specified times and where he can attend and join in the consultation of the surgeon, radiotherapist and pathologist. By this means he would not only give his patient confidence and encouragement but also realize the difficulty in many cases of making a diagnosis. His interest would be aroused and this would make him a very important factor in the subsequent follow-up. He should receive a financial sanction for his attendance. The Regional Centre should see that all practitioners in the whole region are kept informed of the results achieved.

The proposals of local authorities cannot be standardized, but broad principles will be suggested to them if asked for. Each scheme must be modified by the density of population, transport facilities and type of industry.

The schemes are to be sent in by the local authorities, but the medical profession must play its part.

In the words from the Talmud:

"The day is short and the work is great. It is not incumbent upon thee to complete the work but thou must not therefore cease from it."

[January 2, 1946]

DISCUSSION ON ABDOMINAL INCISIONS

Major-General Sir Heneage Ogilvie: My task as opener is merely that of the compère, to make some remarks explaining what the show is about, and to keep the audience quiet while the late-comers are getting into their seats. I will use the Socratic method.

What is an abdominal incision? An incision through the abdominal wall. What then is the abdominal wall? It is the whole edifice that bounds the abdominal cavity, and includes the bony framework, the muscular and aponeurotic walls that enclose it in front and at the sides, the diaphragm that roofs it and the pelvic diaphragm that forms its floor. No consideration of the surgical approach to any abdominal viscus is complete unless we think of it in relation to all these walls, and the value of such three-dimensional thinking has been exemplified during the last few weeks in the discovery by Terence Millin of a new surgical approach to the prostate.

The considerable extension of surgical enterprise that has been made possible by advances in anæsthesia, resuscitation and chemotherapy has encouraged the study of alternative approaches, particularly the trans-diaphragmatic approach to organs in the upper part of the abdominal cavity. I suggest, however, that we should be wise to-day to confine our discussion to methods of approach to the organs lying inside and not behind the cœlomic cavity, and to incisions made through the abdominal walls.

What is the purpose of an abdominal incision? What should it do and what should it not do? An incision should give access to the part to be attacked, and room for the required job to be done. It should be extensible in a direction that will allow for any reasonably probable extension of the scope of the operation. It should interfere as little as possible with the functions of the abdominal wall in the immediate post-operative phase, and it should finally leave it as strong as it was before.

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While the standard incisions I have mentioned can, but very seldom should, be extended to considerable lengths, others are inextensible, being limited either by anatomical confines or by the need to avoid irreparable damage. In the first category are transverse incisions much above the umbilicus which are cramped by the rapidly narrowing epigastric angle, in the second are all vertical incisions near the outer border of the rectus. No surgeon who has seen, as I have, the victim of a full-length incision in the linear semilunaris, the abdominal wall deformed by a large unilateral bulge, the umbilicus in the nipple line, will ever forget the lesson.

The third criterion of a good incision is that it should do the least harm to the abdominal wall itself, to the structures underlying it, and to the patient. In the abdominal

wall nerves matter most, for if they are damaged the muscles distal to the point of damage are paralysed; muscles come next in importance, for they heal by fibrous tissue only, but if the scar is strong and narrow no harm ensues; fibrous and aponeurotic structures matter least, for they repair after division with their own tissue; blood-vessels should be considered, but the arterial anastomosis in the abdominal wall is so free that no proposed incision is likely to be excluded on grounds of the danger of ischæmia. Not only must the structures divided by the knife be taken into account, but the line in which they are divided; when they are cut across their line of strain, stitches pull out and weak areas tend to appear, but when they are cut in that line the edges of the gap tend to be self-supporting, and a few sutures only are needed to approximate them in the immediate post-operative phase.

While avoiding damage to the structures of the abdominal wall itself, a good incision should also take into account the possibility of adhesions to its deeper surface. Adhesions will happen in the best regulated incisions, but whether they are harmful will depend on where they are and what they fix. Fixation of the already fixed matters little; it is only fixation of the mobile that causes symptoms. Adhesions to the colon or liver, that is in the upper or lateral parts of the abdominal cavity, are relatively harmless; those involving the small intestine, that is in the umbilical and hypogastric regions, may be harmful and even dangerous.

Lastly, a good incision must spare the patient. So far I have spoken of the abdominal wall as the first obstacle to surgical enterprise. I must remind you that it is also a prime factor in the maintenance of life and the preservation of health. It maintains abdominal pressure and holds the viscera against the constant efforts of gravity to crowd them into the pelvis. In respiration, it is the recoil mechanism of the diaphragm. In the circulation, it is the counterpart on the venous side of the heart on the arterial side.

Of the abdominal muscles, the recti serve locomotion. They are the flexors of the trunk and opponents of the erector spinæ. Their action is chiefly phasic, and in certain actions, such as rowing, they may be completely relaxed though the abdominal pressure at the time is very high. The rectus sheath has a spatial but not a functional relationship to the muscle. It is the common tendon of the lateral muscles, and is inserted into the linea alba. The strain on it, and the direction of its fibres are almost entirely transverse.

The lateral muscles can act individually in phasic contractions as benders and rotators of the trunk, but as a group their action is postural. They are the maintainers of abdominal pressure and the emptiers of the lungs.

To sum up, the stresses on the abdominal wall are transverse and are constant. The recti are out of action when a patient lies or sits with the trunk and hips flexed, but the lateral muscles maintain their tone and continue their rhythmic contractions while life lasts. Transverse incisions through the lateral parts of the abdominal wall and through the rectus sheath have therefore the support of physiological reasoning, in that they maintain the functions of circulation and respiration unimpaired from the beginning, and of technical requirements in that they are in the line of strain, and after closure they depend little on sutures for their security. Incisions across the rectus muscle have no such sound support, and base their appeal chiefly on giving wide access.

Thus the incisions to which we can give unqualified support are few. Foremost among them are the lateral incisions. These may be strictly transverse or they may be oblique in the line of the nerves, but they should not slope upwards and inwards. They may go as far back as the erector spinæ and as far forward into the rectus sheath as the rectus muscle can be retracted, but they should not cut across it. These incisions increase steadily in popularity. They give excellent access to any structure lying on the same side between the pyloric plane and the pubis. They heal up without incident, they never seem to give way, and they allow unimpeded respiration and coughing from the beginning. Within the last two years they have, in my practice, ousted the lower median and paramedian incisions for all purposes except the most straightforward appendicectomy. For this I still use, as always, the gridiron, which is, after all, the baby of the lateral family.

There are also the vertical incisions in the linea alba or through one or other rectus sheath. They can be any length that the abdominal wall allows, but they should not stray more than an inch from the mid-line. I am tending, like other surgeons of my acquaintance, to abandon incisions that involve the separation of planes and the retraction of layers. Their separated planes leave potential spaces where fluid

may collect and infection may appear and, so far from giving added safety, they are more prone to wound disruption than simpler methods. For this and other reasons I am becoming increasingly attached to the mid-line incision. I used to deplore its limited length, but since I learned from Victor Bonney that the umbilicus is no prohibited area I have cut through that central ornament freely from above or below. The mid-line approach offers the best access to the attics and cellars of the abdomen, and the felted structure of the linea alba gives a better hold for stitches than the anterior and posterior rectus sheaths combined, structures which are all warp and no woof. Since no muscle is cut post-operative pain and therefore respiratory inhibition is less than in the paramedian incisions.

The right and left paramedian rectus-retracting incisions remain standard doors to the abdominal cavity, and very good they are provided they are not used in septic conditions. For these, for an operation on a gangrenous gall-bladder or a gangrenous appendix, I should prefer to cut through rectus sheath and muscle in the same plane.

With regard to closure, I would prefer to seek principles rather than to discuss details. Repair is a function of the tissues, and stitches do no more than bring them into apposition and hold them there while the gap is bridged by living fibroblasts. When there is constant strain on the suture line, stitches, whatever their material, cut through by pressure necrosis and separation follows. Further, there is no "key" layer in abdominal closure; all must be taken into account, and all must heal equally. A chink in the peritoneal suture may lead to wound disruption, or to hernia later. A hæmatoma or a dead space in the rectus sheath may breed an infection that will reach the peritoneum with even greater ease than a peritonitis infects the layers of the incision.

The peritoneum and posterior rectus sheath are usually closed together. Here we seek to provide not only strength, but an unbroken deep surface to which nothing can adhere. A plain over-and-over stitch leads inevitably to inversion and adhesion. In most incisions a continuous everting mattress suture of fine catgut is the best way of closure. In a gridiron incision, the peritoneal opening can be closed by a purse-string, leaving only a dimple on its deep surface.

The muscle layers must be sutured in as many strata as have been cut. In the lateral incisions therefore three layers of suture are required, and, since there is no tension, they may be continuous without reinforcement. In median and paramedian incisions one layer only is closed above the peritoneum, and that a layer divided at right angles to the stresses it-undergoes. Here an unsupported continuous suture is not enough, it should be interrupted, or, if continuous, should be supported by mattress sutures of unabsorbable material. Accurate suture of the skin involves also obliteration of all dead space in the fatty layer. Where deep tension sutures are used they serve this purpose in addition to their primary one; otherwise a series of deep skin sutures must be placed. The actual epithelial apposition is served by Michel's clips or fine edge-to-edge stitches which are removed in three or four days.

I have tried to define a good incision and will now attempt to discuss the poor incisions. There are a number of incisions which are permissible, but which most of us have tried and found wanting. Chief among these are the trans-rectus incisions. The transverse incision across both recti has much to recommend it. It gives the most wonderful access to the upper abdomen. It is physiologically sound, or at any rate based on sound theory, and had therefore an irresistible appeal to every surgeon fresh from the Primary. Its disadvantage is that, the rectus muscle being unsuturable, a space always remains where its fibres are cut, harmless if it repairs by first intention, disastrous if further hæmorrhage or infection ensue. It was a favourite with the magnificent young men who did the forward surgery in the Desert. But the surgeons in South Africa wrote, more in sorrow than in anger: "For God's sake stop your boys from cutting across the rectus; we have never seen such herniæ before, nor in our wildest nightmares have we dreamed them possible."

The Kocher leads us to more acute controversy. It cuts one nerve at most, it does not bleed much, and it usually heals well. I was brought up on it, and I have never admitted abandoning it. I used it last week, and doubt if I shall ever use it again. It gives marvellous access to the fundus of the gall-bladder, which does not interest me, and very poor exposure of that deep Clapham Junction at the liver hilum where ducts join and arteries branch, a region I never approach without anxiety or leave without thankfulness.

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recommended by Pfannenstiel, may be justified at times, but only rarely, and when the diagnosis is beyond doubt. They are, of course, perfectly adequate for the removal of a normal appendix, but we do not spend our lives removing normal appendices.

For an incision to be sightly it should be made with a sharp knife, the skin should be divided at right angles and hæmostasis should be perfect. My only other contribution to a good cosmetic result, is that I excise the scar of a previous operation, if I am opening the abdomen for a second time, so that the patient is left with a single scar.

My standard incision is the paramedian, either right or left, upper or lower abdominal, according to the structure which is to be operated on. In operations on the stomach I prefer the right paramedian for duodenal ulcer, and the left paramedian for gastric ulcer or carcinoma. In resections for duodenal ulcer it is the duodenal end of the stomach which is most likely to be difficult, and a right paramedian incision gives the most direct access to it. In gastric ulcer and carcinoma, a high resection may be called for, and the cardiac end of the stomach can be approached most directly through a left paramedian incision. Paramedian incisions are perfectly satisfactory for colon work, as it must be remembered that when the colon has been mobilized, its mesentery is attached to the central part of the posterior abdominal wall.

For operations for acute appendicitis, I employ a Battle's incision. It has the advantage of not exposing a great deal of the abdomen in the presence of a septic lesion, but its drawback is that it cannot be extended at all easily if the diagnosis is found to be at fault. Should this happen, I close the peritoneum, allow the rectus to fall back into position, extend the skin and anterior rectus sheath part of the incision, and then displace the muscle outwards.

For operations on the biliary tract I use a right paramedian incision in the large majority of cases, and in occasional cases only, particularly in fat subjects, I use a subcostal incision.

In closing my abdominal incisions, I close the peritoneum with a continuous catgut stitch, and if it is at all thin, and seems likely to tear, I pick up a small piece of the under side of the rectus muscle in each stitch to reinforce it. The rectus muscle is allowed to fall back into position; if it is thin and sometimes in the lower part if the incision extends down to the pubes, I fix its inner edge by one or two interrupted sutures to the linea alba. The anterior rectus sheath is closed by interrupted sutures, tension sutures are put through skin, subcutaneous fat and the anterior sheath of the rectus, and finally, the skin edges are approximated with Michel's clips. If a drainage tube has been employed, I put a separate stitch next to it in each layer, so that if it should happen to be eroded no harm results.

I use catgut throughout, except for the tension sutures.

Finally, I put on a sealed dressing, largely to prevent the nursing staff from looking at it. There is no reason for dressing a wound until the clips are removed on the fifth day.

I know that the closure of abdominal incisions is not a matter of the greatest interest to surgeons generally; only too frequently do we leave this part of the operation to our assistants, and even students tend to be bored, and to take no interest in this part of the proceedings. In all circumstances I consider that we should at least close the peritoneum, in view of the importance of this step in its relation to incisional hernia. In addition, if we hand over to our assistants before this is done, there is sure to be a misunderstanding sooner or later, and a swab will be left behind.

I have not attempted to enumerate the various incisions which can be used, but merely to lay down certain principles, and to tell you what I do myself. Surgeons are bound to have individual preferences, as to the way in which they open and close the abdomen.

Professor John Beattie: *Metabolic Changes after Injury.*—Injuries of any kind, whether deliberate or accidental, are followed by a series of changes at the site of injury which are already well known. Less well known, however, are the profound general changes in bodily metabolism which are the inevitable consequences of trauma. Cuthbertson

There are incisions which have the common factor that they divide no muscle but give a wide opening in the mid-line by dividing the anterior and posterior rectus sheath at right angles to each other. These are Pfannenstiel's infra-umbilical and Sloane's supra-umbilical incisions. They are ingenious, and to those who like ingenuity they will make a constant appeal, but it cannot be claimed that they have established any secure footing in abdominal practice.

There are bad incisions too. One that fails on every count, access, extensibility, security, is the Battle. I hope the day will come when the reasons for removing a doctor from the register will move on from the abject A's, alcohol, adultery and advertising, to the baleful B's, Battle and Bassini. A patient who loses his wife can find another; one who seeks treatment in response to an advertisement, either a frank one or a discreet paragraph in the evening press, gets the kind of doctor he asks for; but the man whose abdominal wall or inguinal canal is ruined is indeed betrayed by the profession to which he has entrusted his health.

Mr. Digby Chamberlain: An abdominal incision should: (1) Give adequate access to the structure to be operated on; (2) Leave a firm scar when it has healed; (3) Be as little unsightly as possible.

The satisfactory making and closing of abdominal incisions is as dependent on the anaesthetist as on the surgeon. With good muscular relaxation, it is possible to explore the abdomen in comfort, and to carry out the necessary operative procedures through an incision which might be quite inadequate with a less favourable anaesthetic. My own preference is for an intratracheal intubation, and I find that with it, I get a slack abdominal wall, and that I practically never use a retractor, except the hand of my assistant.

Abdominal relaxation is of further importance in the incidence of incisional hernia. King (1935, *Brit. J. Surg.*, 23, 35) is of the opinion that these hernias and burst abdomens start by the cutting out of the peritoneal stitch, or the escape of a tag of omentum between the stitches during the closure of the abdominal wall. We all know how prone this is to occur in a patient who is straining under the anaesthetic.

It is a fundamental rule that the incision should be adequate; much harm can be done by using too small an incision. Blind manipulations cover a multiple of sins, and it may only be the patient, or the pathologist, at a later stage, who is conscious of their extent.

I remember being very impressed on reading "Fifty Years a Surgeon", by Morris's description of the removal of a stone from the ureter! A small gridiron incision is made in the iliac fossa, through which a finger is put, and the stone is felt on the posterior abdominal wall. With the finger in this position, the patient is rolled over, and a stab wound is made in the back, on to the tip of the finger. The point of the knife in this way opens the ureter and grates on the stone. A pair of forceps is inserted along the knife, and made to grasp the stone, which is then removed. To paraphrase M^{re}chal Bosquet: "It is magnificent, but it is not surgery."

A rapid and systematic examination of the abdominal contents should always be made, before dealing with the organ to which the symptoms have pointed pre-operatively.

The second consideration, that the scar should be firm, depends very largely on the suturing of the peritoneum, and is bound up closely with the anaesthetic. I believe this to be more important than post-operative cough or distension, or the too early return to heavy work. These factors may play a part, but they are much more likely to do so if there is a peritoneal defect, however small it may be.

There are certain factors to which we all subscribe. Nerves should be avoided, and it should not be forgotten that splitting the rectus muscle is bound to denervate its inner part. Blood-vessels are not of great importance, they are so numerous that we cannot seriously interfere with the blood supply of any part of the abdominal wall by dividing them, but bleeding must be controlled as hæmatoma formation favours infection. Muscles are better displaced than divided, although I know that many surgeons habitually, and deliberately, divide certain of the muscles of the abdominal wall.

The third consideration, the cosmetic result, is of small importance. A small incision, lying in a crease and following Langer's lines or a transverse suprapubic incision as

contain all the other essential amino-acids. The success of high protein—high caloric diets in injured Servicemen in speeding up convalescence has been confirmed by many groups of workers in different operational theatres during the last eighteen months of the war.

So far only the effects of injury on otherwise healthy subjects have been considered. The responses to injury in the debilitated human subject are quite different. It matters little whether the cause of debility is tuberculosis, severe infection, high protein loss due to burns, cancer, or starvation. If the debility is extreme, accidental or deliberate wounds do not heal or if they do heal the scars are weak. In Holland before the liberation, surgical work was almost suspended because of the tendency for abdominal and other wounds to remain unhealed often for weeks. Metabolic studies of debilitated individuals who have sustained an injury reveal that there is no increase in the nitrogen excretion during the period when it would be expected were the patient well nourished. Moreover, protein given in any form by any route does not lead to an immediate rise in nitrogen excretion. It would appear that protein is held tenaciously, perhaps as a protective response, to conserve protein needed for the continued existence of the individual. If treatment with high protein—high caloric diets is persisted in, sooner or later the nitrogen output will rise and coincident with this rise normal healing will commence.

Within the past few years it has been discovered that the urine from injured animals and human subjects contains a much increased content of the adrenal cortical hormone—cortin. This hormone has the property of inhibiting the synthesis of protein from amino-acids. Consequently large quantities of these substances are de-aminized in the liver and some non-nitrogenous moieties built up into glycogen. If protein is being destroyed after injury in order to furnish quantities of some essential component, large masses of amino-acids which are not required are set free. If methionine were in fact the essential substance required by the organism, 97% of the protein molecule destroyed would be available for the de-amination and utilization as fuel. The presence of excess cortin enables this utilization to be effected. In debilitated patients cortin excretion is not increased.

Another hormone—testosterone—has precisely the opposite action to cortin. It accelerates the synthesis of protein from amino-acids and hence promotes storage of protein. Protein, however, cannot be synthesized unless adequate quantities of each of the amino-acids needed to build the protein molecule are available. Under conditions of injury the output of testosterone in the urine is diminished. Cuthbertson, Shaw and Young (1941) observed that injections of crude extract of the anterior pituitary gland of the ox into rats which had had simple fractures of the femur prevented the loss in body-weight and excessive loss of nitrogen in the urine which followed such injuries in control animals. Although protein was conserved within the body as the result of such treatment they noted in another series of experiments that skin wounds did not heal more rapidly when the same pituitary extract was administered. Such observations may lend indirect support to the view that protein destruction after injury is effected to set free from the protein molecule some component which is necessary for repair.

The relation between the increased excretion of nitrogen and the excessive production of cortin is by no means clear. In the intact animal, injections of cortin will not induce a negative nitrogen balance. It seems probable, therefore, that the increased nitrogen excretion is caused by the increased cortin production.

It is obvious that the treatment of injury must include some attempt to minimize the effects of the high protein catabolism in the first phase and to produce as high a positive nitrogen balance as possible in the third phase. The aim of this treatment should be to provide a protein intake of not less than 2 grammes per kilogramme of body-weight per day in an otherwise normal human adult, and if possible 2.5 grammes. If the intake can be increased above this level the convalescent period will be noticeably shortened.

The protein intake can be increased by four methods: (a) A high protein diet where the major part (over 75%) of the protein is available from milk, eggs, cheese or meat; (b) the oral use of hydrolysed proteins such as casein or meat; (c) the intravenous infusion of solutions of protein hydrolysates; (d) the intravenous administration of human plasma.

The high protein diet of around 150 grammes of protein per day has also a high caloric value. The total calories should be not less than 2,000, but the ideal is about 3,000 for a

(1929) observed in animals who had simple fractures of the long bones that the amount of nitrogen excreted each day in the urine increased considerably during the two weeks immediately after the injury had been inflicted. Since 1929, and especially during the war years, it has been shown, both in healthy animals and in well-nourished human subjects, that an increased nitrogen excretion is a constant finding after injury. Stevenson and his colleagues (1945) made detailed studies of human subjects suffering from moderately severe injuries and came to the conclusion that the disturbances in nitrogen metabolism fall into three phases. For a period of two to three weeks after the injury the amount of nitrogen excreted far exceeds that taken into the body in food. The nitrogen balance is thus negative. Immediately following this negative phase there is a period of about a week when the nitrogen intake and output just about balance. The third phase, lasting five or more weeks, is characterized by a positive nitrogen balance, i.e. the intake exceeds the output. At the end of this third phase, input and output are approximately equal and the patient may be said to be "recovered".

It is obvious that the excess nitrogen excreted during the first phase of negative nitrogen balance must come from the destruction of body proteins. Normal adults confined to bed and not suffering from any injury or infection lose weight and show an increase in nitrogen excretion. This increased protein destruction can be called the atrophy of disuse. The magnitude of this destruction is, however, not sufficient to account for the amount of nitrogen which appears in the urine after injury. The protein destruction in such cases is an active breaking down of body protein not due to atrophy of disuse.

Nothing is known about the mechanisms which bring about this active protein breakdown (catabolism). They may be presumed to be of a hormonal nature and are set in motion by substances liberated from the damaged tissues. No precise data exist which confirm or contradict such a hypothesis. Various ideas exist as to the meaning of this profound disturbance of protein (nitrogen) metabolism, but here again precise data are lacking. It has been suggested that the breakdown provides the body with a readily available source of energy. If this were so then a diet of a high energy value ought to avert or minimize the amount of body protein destroyed. Trials of such treatments have shown clearly that while some patients show a diminution in the nitrogen excreted the results as a whole do not support the hypothesis. It has been suggested that protein is broken down in order to provide adequate quantities of some protein component which is necessary for the processes of repair. This latter idea has had some experimental support.

Rose and his co-workers (1942) over a period of many years have demonstrated that growth in rats can be halted or retarded when one or more of a number of so-called "essential amino-acids" are absent from the diet. These amino-acids are "essential" in that the animal body cannot synthesize them and that they must be present in the proteins of the food or as the pure substances in artificial diets. Croft and Peters (1945) showed that after experimental thermal burns in rats the negative nitrogen balance which ensues could be diminished markedly when one of the essential amino-acids—methionine—was added to the animals' diet. The deduction from these experiments would thus appear to be that protein is destroyed to secure adequate supplies of methionine. The great protein destruction may be explained by the fact that methionine forms only around 3% of the body proteins. As the protein content of body tissues is about 20% by weight, it would be necessary for 500 grammes of tissue to provide 100 grammes of protein and 3 grammes of methionine. It must, however, be realized that the average human adult weighing around 65 kg. needs about 2 grammes of methionine per day, and if animal experiments are a true guide, growing human subjects would require much more in proportion to their body-weight. It would therefore not be unreasonable to suppose that when the repair processes are active, and they are only but a special type of growth, the methionine requirements of the body may be doubled. Experiments on human subjects suffering from moderately severe injuries have shown that there is a diminution in the rate of protein destruction when doses of 3 to 5 grammes of methionine are given each day during the phase of protein catabolism. Much more accurate and detailed work is needed before it can be stated dogmatically that the excessive protein destruction after injury is an attempt on the part of the organism to meet an increased demand for methionine. When a high protein intake—over 150 grammes per day—is given to patients suffering from severe injuries, the negative nitrogen balance can be diminished until it either becomes negligible or is converted into a positive one. Although the components of such a high protein diet are rich in methionine, they also

Section of Ophthalmology

President—P. E. H. ADAMS, F.R.C.S.

[October 11, 1945]

Penicillin in Ophthalmology. (*Abstract*)

By Professor ARNOLD SORSBY, F.R.C.S.

(1) *Ocular Pharmacology of Penicillin*

A. Tolerance: In the form of drops concentrations up to 2,500 units per c.c. are well tolerated. In ointment form the difficulty so far has been the lack of an adequate base which would not decompose the penicillin and allow of ready absorption. Subconjunctival injections of 600 units in 0.5 c.c. of water are well tolerated and can be repeated daily. Injections into the anterior chamber of quantities of 100 to 200 units are justifiable. Injections into the vitreous are not well borne; the upper limit is probably not much more than 100-200 units. An allergic reaction taking the form of massive swelling of the lids on instilling one drop of penicillin (2,500 units per c.c.) has been observed.

B. Concentration: (1) *Systemic injection*.—On the injection of clinical doses in the rabbit and dog, no penicillin can be recovered from the interior of the eye. These observations have been partly confirmed in man.

(2) *Local applications*.—(a) Drops: No penicillin can be recovered from the interior of the eye in both the experimental animal and in man on the instillation of drops.

(b) Corneal baths and ionization produce a considerable concentration in the aqueous and other ocular tissues of the experimental animal.

(c) The possibilities with lamellæ have not yet been adequately explored.

(d) Ointment bases which damage the corneal epithelium allow a considerable concentration in the aqueous.

(e) Subconjunctival injections of 2,500 units in the experimental animal and 4,000 units in man also allow a fairly high concentration in the aqueous. This is probably not maintained for any length of time.

(f) Injection into the anterior chamber: 500 units injected into the anterior chamber of the rabbit showed the highest level of concentration one hundred and five minutes after injection. Excretion is probably rapid.

(g) Injection into the vitreous: An injection of 5,000 units in man still showed an appreciable amount of penicillin after forty-eight hours.

(h) Modifying factors.

Wetting agents of the aerosol group do not materially affect absorption through the cornea. Absorption is more ready after corneal bath, ionization, and in corneal abrasions and ulcers.

healthy adult. To obtain such an intake, supplementary milk drinks of the type used by Stevenson (1945) are ideal. Protein hydrolysates by mouth suffer from the disadvantage that they are unpalatable unless great trouble is taken to flavour them. They have many advantages. If given by gavage, the fluid and caloric needs of the patient can be met easily at the same time. Moreover, if given over a period of many hours at a slow rate—5 c.c. of 5% solution of the hydrolysate per minute—they are rapidly absorbed and leave no residue. In some patients they are not easily tolerated by the intestinal mucosa and may produce a diarrhoea. Reduction of the total intake by lessening the rate of input often leads to a successful administration. The administration of protein hydrolysates by vein has proved of considerable value in the treatment of the debilitated patient and of patients in whom it is considered unwise to give anything by mouth for a period of days. Suitable preparations, however, are not readily available and some time must pass before any extensive trial of them can be made in civil practice in this country.

In the otherwise normal patient, all the above treatments lead to an increase in the nitrogen output, but it is found that the nitrogen balance is rendered less negative. In debilitated patients, this rise in nitrogen output is not observed. It may be presumed therefore that the nitrogen is conserved as protein. When plasma is given to both normal and debilitated patients the nitrogen output is *not* increased. This whole protein (plasma protein) apparently enters rapidly into the cellular elements and does not participate in the metabolic activities induced by the injury. In cases of injury, except where plasma is used to assist in the restoration of the plasma volume or to replace the loss of whole protein as in burns, plasma infusion is not a method to be used in place of the three methods already mentioned. If it be true that the increased protein metabolism in injury provides adequate supplies of some protein constituent necessary for the repair process, then whole plasma protein by vein must be broken down before it can supply this constituent. The most economical way to provide this hypothetical constituent would seem to be by a proper diet and failing that by hydrolysed proteins given by mouth or by vein.

The treatment of the debilitated patient is identical with that of the otherwise normal, except that the intake must be made as high as possible if convalescence is to be rapid and healing sound. Successful treatment is followed after a few days or a week by a gradual rise in nitrogen output. Maintenance of a high nitrogen input until healing is well advanced is essential.

The use of vitamins to accelerate healing has been investigated by numerous observers. Vitamin C (ascorbic acid) is one vitamin which seems to be concerned intimately with the repair process. After injury this substance disappears from the urine and cannot be made to reappear even when large quantities of it are administered. It is known that it is concerned in some way with the formation of cortin, and it is also essential for the production of collagen so necessary for the development of strong scar tissue. The level of intake of ascorbic acid should be at least twice the accepted optimum for adults.

It has not been possible in this paper to mention the many groups of workers who have contributed so much to our understanding of one aspect of the effects of injury. The various conferences in New York on wound healing convened under the auspices of the Macy Foundation have been a great stimulus to those of us in this country who have investigated some of the problems of wound healing. Although much has become known since 1939, we are still a long way from understanding the fundamental mechanisms involved in the healing of even a clean surgical wound.

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Mr. L. H. Savin asked how frequently an allergic response was seen. He added that he was not wholly convinced about the trachoma case, because he had seen rapid improvement occur in trachoma under ordinary methods. Was any other treatment adopted at the same time as the penicillin?

Mr. R. Lindsay Rea had had a case of a man discharged from the Army with multiple thromboses throughout his body—arms, legs and chest—and on examination he found a central scotoma had just developed in one eye. The dental radiographs showed the teeth to be extremely infected and Dr. Bodman suggested that during the removal of the teeth he should have at the same time heparin and penicillin drip given intramuscularly to prevent a further thrombosis as the clotting time of the blood was so low—with the result that no untoward happening took place and the scotoma was reducing in size.

He had always felt some trepidation in an eye case when teeth had to be removed wholesale and it was well to know that penicillin could be used as a drip during the time of and immediately after the dental operation.

Professor Sorsby said he had been asked whether ionization had been tried in septic inflammation of the eye. In a case—reported by Dunnington and v. Sallmann—of post-operative infection of the eye which was treated by ionization together with systemic administration, the condition cleared up.

No one could speak with certainty as to the effective concentration of penicillin, as there was a difference in the susceptibility of different organisms. What was an effective concentration in one case would not be the effective concentration in another. What they could aim at was to use the maximum concentration tolerated by the eye and hope that that was effective.

Professor Riddell had taken him up on the question of sulphonamide in local infections. He was criticizing the figure as regards the effect of penicillin in ophthalmia neonatorum, particularly the virus infections. The following were the actual figures: 15 virus cases successfully treated with 2,500 units; these were cases which cleared up within from half an hour to ten hours without any relapses; 4 cases relapsed after an initial success; no case was a total failure. In a total of 98 cases of ophthalmia neonatorum due to various causal organisms, the relapses amounted to about 13%, very similar to the percentage obtained in about 700 cases treated with the sulphonamides.

Mr. Greeves had raised an important theoretical point. Professor Sorsby agreed that even if penicillin did not penetrate into the interior of the eye, it might still be of value. It was the ciliary body which held back penicillin from reaching the interior of the eye. He had no definite knowledge of the concentration of penicillin in the ciliary body, but by analogy with the choroidal plexus he thought it might be extremely high, and it was likely that a good deal of this diffused back into the choroid; it was thus possible that choroidal infection would be influenced. The experience of other observers, however, was on record, and most of them had failed to obtain any improvement in choroiditis. The question arose at what stage the choroiditis was treated and the character of the organism. More experience was wanted.

He had been interested to hear Mr. Purvis's account of failure with drops in blepharitis. He himself did not use drops, but painted a solution of penicillin on the lid margins.

In the whole of his experience, which must have embraced considerably more than 500 cases, he had seen allergic response only once. He agreed with Mr. Savin in his criticism. He was not saying that penicillin cured trachoma, but he was reporting it as a possibility to be explored. Treatment in that particular case was exclusively with penicillin, apart from the expression.

[November 9, 1945]

Neuro-retinitis of Unknown Origin.—NIGEL CRIDLAND, D.M.

Mr. Cridland said that he had seen the patient who was 24 years old in Colombo three years ago and had been hoping to obtain an opinion on it ever since. The original complaint was a diminution of the field of vision. There was no clue to the cause and the fundus was normal when first examined. At that time, six months after the onset of symptoms, the field to 5/320 white was reduced to 5° from the fixation point. Visual acuity was 6/5.

Three months later, as no cause had been found, he trephined the right eye in the hope of increasing the retinal circulation and so of arresting, or at any rate, delaying the field loss (which had reached the figure of 3° from the fixation point at the time of operation).

After recovery from operation the field was 23½°, central vision was 6/5 corrected and the field had remained unchanged from that time until now. Central vision was also unaltered after operation. The only fundus abnormalities were a few fine flecks of pigment along the inferior nasal vein and a suggestion of a very mild diffuse retinal oedema.

To-day the fundus appearances were those of a fine diffuse chorio-retinitis.

Mr. Cridland said that the only possible cause which had appeared in the history was two courses of sulphapyridine given for gonorrhœa but he was very doubtful of the significance of this and he invited comment or suggestions as to ætiology. It was, however,

(2) *Penicillin in Experimental Infections*

(1) *Corneal infections*.—There is no adequate experimental lesion of the cornea for testing the value of penicillin in its various modes of application.

(2) *Inoculation into the anterior chamber*.—The use of corneal baths and ionization after infecting the anterior chamber with pneumococcus and *Staphylococcus aureus* gave mostly satisfactory results.

(3) *Inoculation of Staphylococcus aureus into the vitreous*.—Systemic administration of penicillin gave no results. Injection of penicillin into the anterior chamber and subconjunctivally produced some control. Injection into the vitreous gave good results, the best being when quantities of more than 1,000 units were used.

(3) *Clinical Findings*

(1) *Systemic administration*.—Reports are conflicting. Cures in reported cases have largely been in external infections (ophthalmia neonatorum, gonococcal conjunctivitis). Intraocular infections have mainly not responded.

(2) *Local applications*.—A large number of reports give satisfactory results with solutions and ointments in blepharitis, acute conjunctivitis and superficial corneal ulcers. Good results have also been obtained in hypopyon ulcer. Reports on treatment of infected socket are conflicting.

(3) Irrigation of an infected anterior chamber and the injection of penicillin in such lesions have given good results.

(4) *Subconjunctival and intravitreal injections*.—No adequate data are as yet available.

(5) Penicillin in the form of drops has been used for a series of 123 cases of ophthalmia neonatorum. The best results are obtained with a concentration of 2,500 units per c.c., the drops being given at frequent intervals. When instilled at one-minute intervals purulent discharge is controlled within half an hour.

(6) The possible use of penicillin in trachoma and interstitial keratitis is indicated on the basis of a small series.

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Mr. D. V. Giri asked whether ionization of penicillin had been tried in septic inflammation of the interior of the eye or in septic inflammation arising after operations for cataract. What was the effective concentration of penicillin which should be used?

Prof. W. J. B. Riddell asked why parenteral administration should not be given at a high level to ensure that penicillin did penetrate the eye. Was it still a question of supply or was there any technical reason against it?

He considered that there was a potential danger in ointment bases being used for lowering surface tension or lowering interface tension. These detergent mixtures might well cause damage to the eye, and care must be taken in dealing with such substances.

He did not consider that full justice was given to the work of Robson and Scott. The lesion they produced was a reasonably standard one. Granting that it did not lead to the destruction of the eye, it was still of great importance in research into eye conditions if the time of healing could be accelerated. It was very advantageous if this could be achieved by the use of penicillin.

Mr. R. Affleck Greeves said that the fact that penicillin administered systemically did not appear in the aqueous did not necessarily mean that it did not penetrate the tissues of the uveal tract and retina. He quoted 2 cases in point, in which syphilitic uveitis and retinitis respectively had quietened down after the systemic use of penicillin. He knew, of course, that many intra-ocular inflammations were probably allergic rather than bacterial, but even so blood-borne penicillin might conceivably operate by attacking a distant septic focus of infection. He also desired to ask whether there was any evidence that penicillin given systemically could penetrate the cornea. He had had one case of hypopyon ulcer which he treated with penicillin in that way and which did extremely well.

Mr. V. B. Purvis said that they all hoped that penicillin would help in cases of intra-ocular infection, although, as Professor Sorsby had pointed out, penicillin did not enter the interior of the eye. Might there not be some indirect effect? Had not the time come when they might be recommended to use penicillin before an eye operation? He had not been successful with drops in the treatment of blepharitis. A technical point was that the ointment base with which they were often supplied went hard and to that extent was unusable. In general the effect of penicillin was remarkable. While it might have no direct effect, he had found it most helpful in intra-ocular infections.

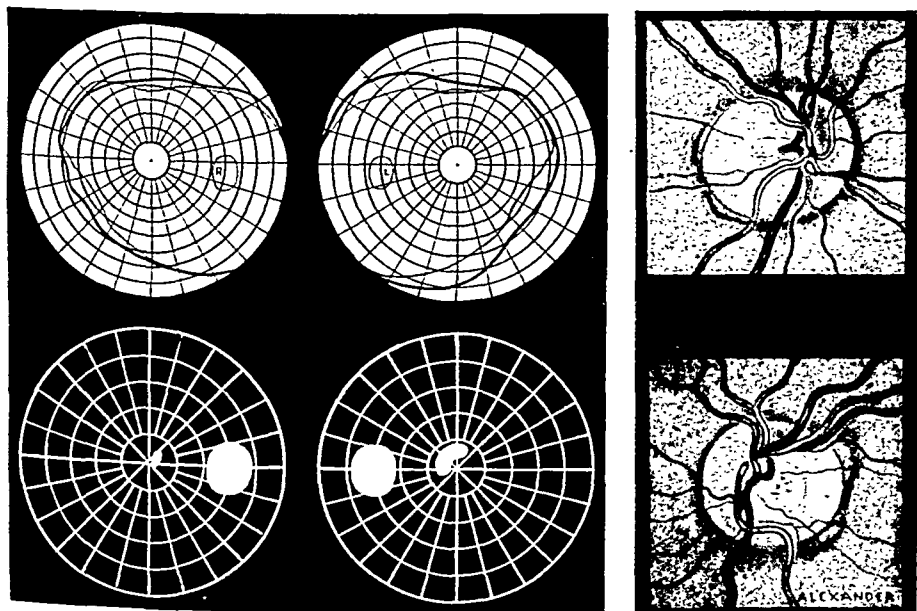
vitamin B tablets which were issued by the Japanese and he also managed to buy some ten eggs monthly.

His vision failed quite quickly—over a period of two days—in December 1942, and then recovered slowly during the following year after which he was of the opinion that it had remained stationary.

When seen on June 6 last he had temporal pallor of both discs and central vision was reduced to 3/60 in the right and 6/36 in the left eye—both not improved, but peripheral fields were full to a 2/330 white target. I referred him to Lieut.-Colonel Hargreaves i/c Medical Division at Millbank as a case of nutritional retrobulbar neuritis and he agreed with me that the optic atrophy was the result of malnutrition. No other physical signs of disease were found in this patient apart from the pallor of the discs and some dental caries and as he was eager to return to his home in Canada for domestic reasons he was allowed to proceed without further delay.

CASE II.—Sgt. D. G., aged 29, who was admitted to Shenley Military Hospital on July 18, 1945. He had been taken prisoner at Mulmein, Southern Burma, on May 19, 1942, was kept there for a month and then moved to Rangoon where he remained until he managed to escape a few days before the 14th Army reoccupied that city, reaching the British lines on May 12, 1945.

At Mulmein his diet consisted almost wholly of polished rice with a little bean soup. At Rangoon the diet was more plentiful but for the first twelve months consisted largely of rice with a small amount of vegetables (potatoes, marrow, cucumber, pumpkin), and lesser quantities of meat and sugar. Thereafter the prisoners' rations were increased somewhat, they received more meat, and rice sweepings were added to the diet.



Sgt. D. G. (November 1, 1945). Showing peripheral fields to a 1° white object, paracentral scotomata and blind spots to a 2/1000 white target and pallor, mainly temporal, of the optic discs.

On July 14, 1943 (his birthday!) whilst reading a book his vision suddenly failed and he was unable to finish the novel. For three months prior to this he had been suffering from pain and numbness in his legs and had experienced some difficulty in balancing himself; there was no swelling of his ankles. He was in a hospital (of sorts!) at the time of his visual loss receiving treatment for dysentery. The pain and numbness in his legs improved slightly with the addition of rice sweepings to his diet, but he did not notice any change in his vision. He had been wearing glasses for the correction of a small degree of myopia prior to his capture but these were taken from him by the Japanese.

He was in hospital in India in June, and the first half of July 1945, and was then evacuated to the U.K. by air. I first saw him on July 19, 1945, the visual acuity of the

right eye was then $< 6/60 \text{ e} - 3.25 \text{ sph.} = 6/60$, that of the left $< 6/60 \text{ e} - 0.50 \text{ sph.} = 6/60$, — peripheral fields full, scotometry was unreliable as the patient could not fixate and the fundi showed fairly generalized pallor of the discs. He was put on a full diet with three multivite tablets three times a day to date and in addition received injections of Benerva—25 mg.—daily for seven days in July and a further course of Benerva injections for a fortnight in October 1945.

Sgt. D. G. is of the opinion that his vision has improved since his return to this country and on November 1, 1945, his corrected vision was R. 6/36 and L. 6/24, peripheral fields were full, scotometry showed paracentral defects and the discs no appreciable change.

remarkable that the field had remained unchanged for three years after operation despite the enormous early loss.

Mr. E. F. King thought this was a case of widespread superficial choroiditis. The changes in the retina were secondary.

Ocular Myiasis.—R. J. V. PULVERTAFT, M.B.

Myiasis affecting the eye is stated to be not uncommon in the natives of Upper Egypt. Three cases were noted in British troops in the Tel-el-Kebir area, in a period of nine months.

The first two cases were very similar, the patient complaining that he had had a "fly in the eye" and could not get it out. On examination minute larvæ were found in the conjunctival sac. [A photomicrograph of one of these was shown.]

The third case was a patient suffering from a blind, painful eye resulting from a battle injury. After removal the eye reached the laboratory, and when cut open revealed a fully developed larva in the posterior chamber.

The conjunctival larva was provisionally diagnosed by an entomologist as *æstrus* ovis.

It is stated that cases of conjunctival myiasis were also recorded in the Alexandria area.

Mr. A. F. MacCallan said that they were indebted to Dr. Pulvertaft for exhibiting the photomicrograph of a larva from the conjunctival sac and the specimen showing a larva in the posterior chamber. [Not published.] The identification of the conjunctival larva as that of *æstrus* ovis was of interest as it had not previously been reported in the *Bulletin of the Ophthalmological Society of Egypt* as infesting the eye. *Onchocerca volvulus* had been reported by Barrada (1934) at the macula; an illustration of the case was shown in Duke-Elder's Textbook. Extra-ocular infestation by *Filaria bancrofti* had been reported by Sobhy (1922).

Every year a number of patients with ocular myiasis or fly-blown orbit were seen at the Egyptian ophthalmic hospitals. These had all been due to *Wohlfartia magnifica*, an arthropod. This fly was viviparous, settling on the conjunctiva for a fraction of a second it deposited active larvæ which started burrowing in the fornices at once. Children and elderly or infirm persons were usually attacked. The conditions produced were sometimes terrible. A single case of bilharziasis of the conjunctiva had been reported by Sobhy.

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Mr. Frank Juler asked how the fly got inside the eye.

Dr. Pulvertaft replied that the maggot actually ate its way through to the sclera or cornea.

Myotonic Pupils with Unilateral Myosis on Drinking Cold Water.—JAMES CRAN, M.B., Ch.B. (introduced by Mr. EUGENE WOLFF).

Dr. Cran said that this was the case of a woman aged 21, first seen on July 5, 1945. She had contraction of the left pupil on drinking cold water. The patient was seen by Mr. Wolff on the same day who reported that vision was normal, fundi were normal; the pupils were central, circular, equal, did not react to light, but reacted very sluggishly to convergence.

Although the patient might have myotonic pupils knee-jerks could be elicited on reinforcement.

No other abnormality was found on complete physical examination.

The Wassermann reaction was negative.

Mr. Eugene Wolff said that it was extremely difficult to see how the reflex could have any relation to the 3rd nerve.

Dr. Cran, in reply to questions, said that he understood the same reflex was not forthcoming to warm water. Moreover, it was elicited only when the water was actually swallowed, not when it was held in the mouth.

Nutritional Retrobulbar Neuritis

By LIEUT.-COLONEL C. DEE SHAPLAND, R.A.M.C.

A NUMBER of our prisoners of war now returning from Japanese prison camps show signs of a past retrobulbar neuritis, almost certainly nutritional in origin, and as this condition does not appear to have been widely recognized in this country the demonstration and description of a few cases may be of interest.

CASE I.—Was seen at Millbank on June 6, 1945.

Major N. I. M., aged 38, of the I.M.S., had been captured by the Japanese in February 1942, and set free when the 14th Army entered Rangoon. His diet from February 1942 to May 1945 consisted mainly of polished rice with very occasional vegetables, dried fish and pork. During the last two years of his captivity he was able to get yeast and

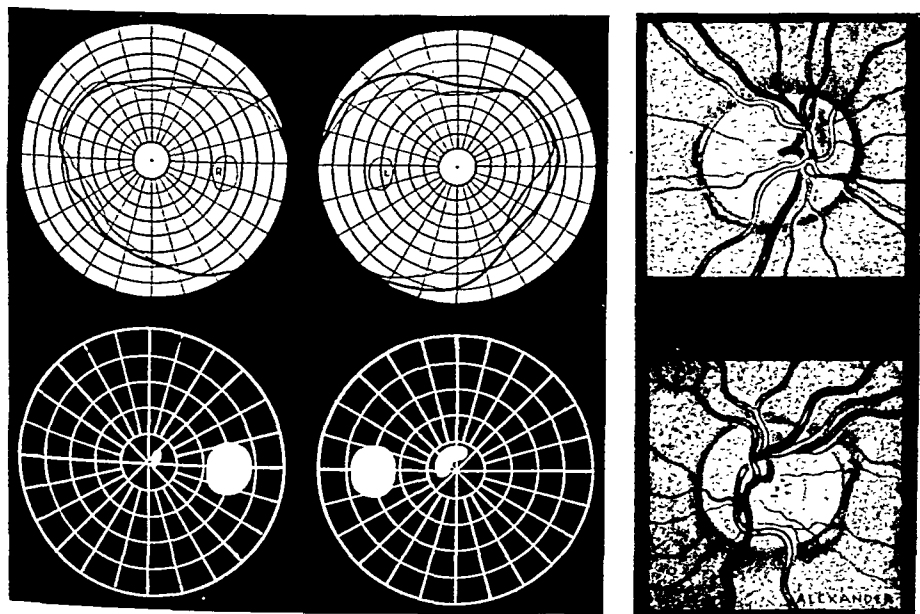
vitamin B tablets which were issued by the Japanese and he also managed to buy some ten eggs monthly.

His vision failed quite quickly—over a period of two days—in December 1942, and then recovered slowly during the following year after which he was of the opinion that it had remained stationary.

When seen on June 6 last he had temporal pallor of both discs and central vision was reduced to 3/60 in the right and 6/36 in the left eye—both not improved, but peripheral fields were full to a 2/330 white target. I referred him to Liéut.-Colonel Hargreaves i/c Medical Division at Millbank as a case of nutritional retrobulbar neuritis and he agreed with me that the optic atrophy was the result of malnutrition. No other physical signs of disease were found in this patient apart from the pallor of the discs and some dental caries and as he was eager to return to his home in Canada for domestic reasons he was allowed to proceed without further delay.

CASE II.—Sgt. D. G., aged 29, who was admitted to Shenley Military Hospital on July 18, 1945. He had been taken prisoner at Mulmein, Southern Burma, on May 19, 1942, was kept there for a month and then moved to Rangoon where he remained until he managed to escape a few days before the 14th Army reoccupied that city, reaching the British lines on May 12, 1945.

At Mulmein his diet consisted almost wholly of polished rice with a little bean soup. At Rangoon the diet was more plentiful but for the first twelve months consisted largely of rice with a small amount of vegetables (potatoes, marrow, cucumber, pumpkin), and lesser quantities of meat and sugar. Thereafter the prisoners' rations were increased somewhat, they received more meat, and rice sweepings were added to the diet.



Sgt. D. G. (November 1, 1945). Showing peripheral fields to a $\frac{1}{2}^\circ$ white object, paracentral scotomata and blind spots to a 2/1000 white target and pallor, mainly temporal, of the optic discs.

On July 14, 1943 (his birthday!) whilst reading a book his vision suddenly failed and he was unable to finish the novel. For three months prior to this he had been suffering from pain and numbness in his legs and had experienced some difficulty in balancing himself; there was no swelling of his ankles. He was in a hospital (of sorts!) at the time of his visual loss receiving treatment for dysentery. The pain and numbness in his legs improved slightly with the addition of rice sweepings to his diet, but he did not notice any change in his vision. He had been wearing glasses for the correction of a small degree of myopia prior to his capture but these were taken from him by the Japanese. He was in hospital in India in June, and the first half of July 1945, and was then evacuated to the U.K. by air. I first saw him on July 19, 1945, the visual acuity of the right eye was then $< 6/60 \text{ } \varepsilon - 3.25 \text{ sph.} = 6/60$, that of the left $< 6/60 \text{ } \varepsilon \xrightarrow{-3.50} \xrightarrow{-0.50} = 6/60$, — peripheral fields full, scotometry was unreliable as the patient could not fixate and the fundi showed fairly generalized pallor of the discs. He was put on a full diet with three multivite tablets three times a day to date and in addition received injections of Benerva—25 mg.—daily for seven days in July and a further course of Benerva injections for a fortnight in October 1945.

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CASE III.—Pte. L. Frank, aged 25, was referred to me by Major Mrs. Stewart from the Royal Herbert Hospital, Woolwich, on September 9 of this year. He had been taken prisoner by the Japanese in April 1943, and was in Rangoon for just two years before being set free on April 30, 1945.

His vision failed in both eyes in December 1943, since when there had not been much recovery. During the middle twelve months or so of his captivity he had experienced difficulty in walking and much pain in his toes.

He showed temporal pallor of both discs with vision reduced to 6/36 in the right and 1/60 in the left eye, both not improved. Peripheral fields were full but the right showed a pericentral and the left a central scotoma—absolute—to a 1/330 white object. Blood Wassermann and Kahn were negative. X-ray of the skull showed the sella turcica and the remainder of the skull to be within normal limits and there was no evidence of raised intracranial pressure. There was no confirmatory evidence of disseminated sclerosis.

His diet as a P.O.W. was largely polished rice and there seems no doubt that he had suffered from "dry" beri-beri complicated by a nutritional retrobulbar neuritis.

Since the arrival in this country in the last two weeks of October 1945 of a number of transports bringing repatriated prisoners mainly from Singapore several further examples of this condition have been seen at Millbank amongst whom was Captain E. D. H. Williams, aged 33, of the R.A.M.C. He was taken prisoner at Singapore on February 15, 1942, and was in the prison camp at Changi on Singapore Island during the whole of his captivity. His staple diet was polished rice but with additions. His vision began to deteriorate early in May 1943, and at the end of the month the acuity was about 6/9 R. and L. but with small pericentral scotomata. He was put on 4 oz. of rice polishings a day but this gave him severe diarrhoea and a fortnight later his central vision had gone down to 6/60 in each eye. An ounce of marmite a day was then substituted for the rice polishings with considerable improvement to his visual acuity which in about a month had risen to 6/18 R. and L. From June to September 1945 Captain Williams suffered from angular stomatitis and had some transient oedema of the ankles.

When seen at Millbank on October 29 last his central vision was 6/18 pt. R. and L. not improved, the media of both eyes were clear and the fundi normal except for slight temporal pallor of the discs; peripheral fields were full and there were small pericentral scotomata.

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With regard to changes in the visual field Elliot states that these would appear to vary very greatly in different cases. Many writers make no reference to any constriction of the peripheral fields either for white or for colours, indeed Coppez went out of his way to record that peripheral vision was undamaged in his case. Ishihara stated that contractions of the visual field occur, but were transitory in nature, whilst Yamaguchi found no marked contraction of the white field, but that those for red and green were shrunken. It is of interest in this connexion to note that though atrophy of the papillo-macular bundle is of not infrequent occurrence in these cases, a general optic atrophy is apparently quite rare.

Later work and observations, more especially by Fitzgerald Moore (1945) in West Africa and by H. S. Stannus (1944) in this country, have led to the view that the type of retrobulbar neuritis here described is part of a syndrome characterized by sore tongue with cracked lips, dry furfuraceous skin, dry scaly scrotum and by various nervous manifestations, which, apart from loss of visual and auditory acuity, consist of mental dullness, a sense of muscular weakness, ataxia and paræsthesiæ, the whole syndrome

being ascribed largely to riboflavin deficiency, though probably other factors of the B complex are involved.

As regards treatment Fitzgerald Moore found it worth while to treat all cases having a history up to twelve months. Over that period improvement was problematical unless the patient was still suffering from subacute effects of his malnutrition. Cases in which a diminution of vision had become manifest in less than a year generally showed a good prognosis and those with a history of six months or less an excellent one. He gave 1 oz. of marmite a day and continued this high dosage over a period of at least six months. In favourable cases visual response commenced within three to six weeks, usually about "One Snellen line a fortnight", others were much slower while a considerable number had reached an irreversible stage and did not improve. Occasionally, however, unexpected and un hoped-for results were obtained in cases where all the signs suggestive of irreversible changes had intervened and for that reason alone he was of the opinion that persistence in treatment was always justified.

Fitzgerald Moore also points out the importance in these cases of better class and more varied carbohydrates and stresses the danger of certain staple carbohydrate foodstuffs such as rice, manioc, sago and sugar-cane when eaten to excess where the general dietary itself is poorly balanced.

Many of the patients I have seen found that their symptoms, including loss of visual and auditory acuity, were temporarily exacerbated following their liberation and the subsequent institution of a full diet. This, with further observations, was noted by Captain E. D. H. Williams who was a prisoner himself at Changi for three and a half years.

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Captain E. D. H. Williams, who had been for three and a half years a prisoner at Changi, said that possibly the circumstances of the captivity itself accounted for a rather defective memory.

The main carbohydrate diet the whole time was rice. During the first year they had up to 20 oz. a day, but later it was cut down to 14 oz., and that went on for a further six months until 1944 (June). During the next six months there was a slight improvement, but by Christmas 1944 they were very short of rice. Substitutions for this diet were meat, and there was a good deal of mutton and beef available for the first nine months, and they had a fair proportion of that meat. Afterwards fish was almost the only protein available, including something called whitebait (which, however, did not taste like it), and of this they had about 1 oz. a day, usually rather less. After the first six months they got some Red Cross goods—bully beef and milk—and again a year later, and again in June 1945 a more varied quantity, with a certain amount of fish, cheese, butter—and rice! At one period a certain number of sardines became available, and these seemed to have a good effect on the people generally. The black period was after Christmas 1942. Green vegetables grown by the captives were sometimes available, but the supply of these depended upon whether the camp was moved or not. At the beginning of 1944, under the influence of the Americans, maize was cooked in wood ash, and, whether as a consequence of this or not, a large number of people developed what they thought to be pellagra. Neuritic beri-beri started early and was seen particularly in people who had taken a large quantity of alcohol. Later on it appeared to be connected with people who got dysentery, and later still it became so complicated that nobody knew what its cause was. The oedematous form of beri-beri started rather later, and seemed to be connected in certain cases with achlorhydria. Some dozen cases of spastic paraplegia he saw seemed to be permanent with one marked exception. One post-mortem showed the white matter of spinal cord studded with necrotic areas the size of millet seeds. These deficiencies did not seem to be connected with retrobulbar neuritis, but this was apparent in a second group of cases in which there was what was considered to be riboflavin deficiency. Scrotal dermatitis was seen very frequently. The severe conditions were seen starting again about February of this year and reaching their height in August and September, when people were found dying suddenly. With the return to normal food the eye conditions did not worsen as did oedematous and cardiac forms of avitaminosis.

Mr. M. L. Hine said that only the previous week he had seen a civilian who had returned from Hong Kong, and who told him that a few months after being in the camp he had central blindness and could not read at all for some months. The Japanese gave him some vitamin tablets. When he mentioned to him the name "nicotinic acid", he recalled that they gave him some of that too. He recovered, and, when he was seen, his fundus was normal and vision 6/5 with no scotoma. This confirmed what Colonel Shapland had said about the good outlook if treatment were early enough.

Dr. R. J. V. Pulvertaft said that there was an epidemic of this sort in the British war camp at Suez. An attack of pellagra in Libyan and German prisoners was attributed to illicit stills which were thought to be making methyl alcohol. The case was investigated, but it seemed from the evidence to have been a true dietetic deficiency. In May

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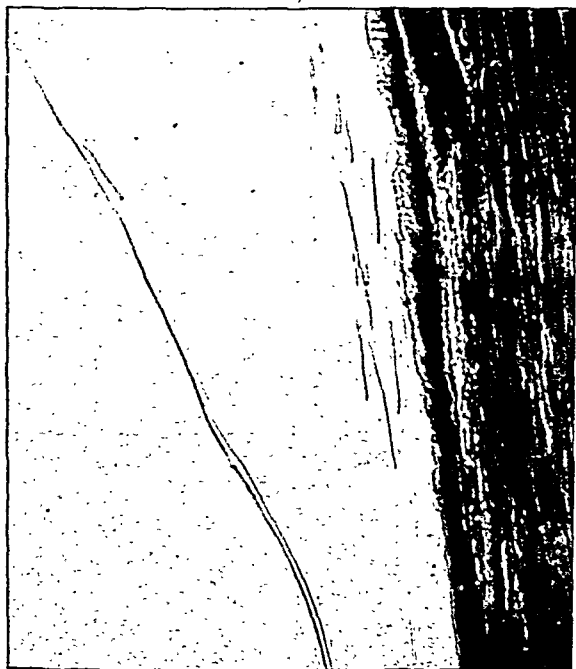
Fig. 2 shows a zonular fibre becoming continuous with the zonular fibre of the anterior capsule.

This fibre is one of the orbiculo-anterior capsular fibres, the longest and strongest fibres of the zonule. They arise from the pars plana and receive auxiliary fibres along their whole course. They lie in the valleys between the taller ciliary processes, where they form well-marked bundles.

Most of the auxiliary fibres run from behind forwards and inwards, but just behind the posterior ciliary processes they also run from in front backwards and inwards. The zonular fibres here, therefore, have a double attachment which makes for strength and so it is usually just beyond this point that the fibres break.

Are there any equatorial fibres? The answer lies in the development and natural history of the zonule.

(a)



(c) (b)

Pars plana Sclera

FIG. 1.—Orbiculo-anterior capsular fibres (a); also orbiculo-posterior capsular fibre (b) in close relation with anterior limiting layer of vitreous (c). $\times 250$. Ant. post. section. (Zenker, Mallory's triple stain.)

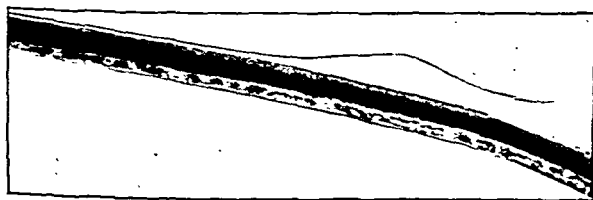


FIG. 2.—Zonular fibre becoming continuous with the zonular fibre of the anterior capsule. $\times 250$. Ant. post. section.

In the embryo and at birth there are a great many more fibres than in the adult. These arise not only from the inner aspect of the ciliary body but from the back of the iris, the angle of the posterior chamber and from the most anterior ciliary process which in the adult lies free from zonular fibres. Also on the lens capsule the space between the anterior and posterior groups of fibres is entirely filled in by equatorial fibres. With age, many of these equatorial fibres disappear and only a few sparse ones or none at all may

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Elliot in his *Tropical Ophthalmology* (1920) from which source the above Japanese references were obtained states the signs of retrobulbar neuritis fall under three headings: (1) central scotoma, (2) diminution of the central visual acuity, and (3) changes in the visual field. In the earlier stages, the scotoma is of small size, and according to Miyashita it is connected with the blind spot by a narrow bridge, thus giving it what he speaks of as "its most characteristic pestle-shaped form". Ishihara described the defect as having an irregular, elongated oval form in one case and as being half-moon-shaped in another, whilst Aoki described the white and colour scotomata as nearly always obliquely oval and added that the size of the latter diminished in the order, green, red and blue.

According to Miyashita whilst the scotoma enlarges, the central vision gradually falls till it reaches the low limit of 6/60; he adds that it seldom goes lower than this. It is this interference with vision which leads the patient to seek medical relief, and thus results in the recognition of the diagnostic sign of central scotoma.

With regard to changes in the visual field Elliot states that these would appear to vary very greatly in different cases. Many writers make no reference to any constriction of the peripheral fields either for white or for colours, indeed Coppez went out of his way to record that peripheral vision was undamaged in his case. Ishihara stated that contractions of the visual field occur, but were transitory in nature, whilst Yamaguchi found no marked contraction of the white field, but that those for red and green were shrunken. It is of interest in this connexion to note that though atrophy of the papillo-macular bundle is of not infrequent occurrence in these cases, a general optic atrophy is apparently quite rare.

Later work and observations, more especially by Fitzgerald Moore (1945) in West Africa and by H. S. Stannus (1944) in this country, have led to the view that the type of retrobulbar neuritis here described is part of a syndrome characterized by sore tongue with cracked lips, dry furfuraceous skin, dry scaly scrotum and by various nervous manifestations, which, apart from loss of visual and auditory acuity, consist of mental dullness, a sense of muscular weakness, ataxia and paræsthesiæ, the whole syndrome

Plastic Artificial Eyes

By Squadron Leader F. J. STEWART, R.A.F.

SQUADRON LEADER STEWART spoke briefly on the subject of plastic eyes. His experience in plastics up to four or five years ago had been confined to plastic dentures and plastic teeth, but his observations from R.A.F. patients with glass eyes suggested that plastics might be used in these cases with considerable advantage.

He briefly enumerated some ten defects of the glass eye, such as fragility, surface erosion, imperfect fit, light reflection, weight, &c. Plastics on the other hand, he claimed, overcame these difficulties, and two or three years' tests in patients' sockets confirmed this. Against plastic eyes there was always the possibility of a person having an idiosyncrasy to the material (methyl methacrylate) though no case had occurred in some two or three hundred cases that he had studied; in American literature it was stated that it existed in one in ten thousand.

With present technique the cost of acrylic eyes was considerably more than glass as it involved the taking of impression and building up each eye individually. Plastic eyes were being mass produced very cheaply, though by this means many of the advantages of plastic were lost, but on the grounds of permanence and lightness plastic still had advantages over its glass counterpart.

Specimen cases of glass eyes and their defects and plastic eyes in the various stages of construction to the finished article were on display.

Mr. D. V. Giri asked what it would cost a patient to have a plastic eye made for him. At the Southern Ophthalmological Society two weeks previously a patient was demonstrated who had been fitted with a plastic eye which was a marvellous match, so that it seemed there were people already making plastic eyes. With regard to the time for which glass eyes lasted, not very long ago he had come across a patient who had kept the same eye for eight years, and it was a wonderful match.

A Visitor asked who it was proposed should make these plastic artificial eyes in the future. The author had said that the eye might be taken out and washed. It had fallen to his lot to provide skin linings for sockets, and he had always been troubled by the amount of discharge. The discharge seemed to increase when the artificial eye was inserted. This discharge might last a long time, and it was one of their great difficulties to stop it. Was any experience available concerning the supply of eyes to skin-lined sockets? Had such skin linings any disadvantage?

Dr. Margaret Dobson asked whether the material used for plastic artificial eyes was the same as for plastic lenses. She knew little about plastic artificial eyes but a good deal about plastic lenses. She had ordered quite a number of them and wore plastic spectacles herself. The trouble was that they scratched so very easily. She recalled that one of her duties in the first European war was to do a good deal of fitting for glass eyes, and that and subsequent experience made her stand up for the glass eye, which might be beautifully made and most comfortably fitted, if made for each individual case by an expert. Mass-produced eyes were often found to fit badly.

Mr. Victor Purvis said that he was reminded of a case he saw last year, that of an old agricultural labourer who had worn an artificial eye continuously in the same socket day and night and had never taken it out for fifteen years. He had now broken the eye and wanted to know what he should do with the remnants in the socket.

Mr. Frederick Ridley said that he had had experience in the Facio-maxillary Unit at East Grinstead during the war in connexion with the reconstruction of sockets in order to carry a prosthesis. It was found that it was first necessary to distend the socket and to keep it distended. Too little attention was often paid to the preparation of the socket for the eye. Unless the patient had been wearing an adequate glass shell or some form of prosthesis one's first duty was to distend the socket if a good cosmetic result was to be obtained, otherwise the eye would appear unnecessarily small. The author had raised the question of motility. At East Grinstead they found that the best thing to do was to use a prosthesis as a temporary filling which had a conical hollow at the back, rather like the shell eye with which they were familiar. If there was a hollow in the back of the prosthesis, the soft tissues were easily moulded so that a mobile stump or cone, as it was called, was very quickly formed; this cone contains the ends of the muscles. Over this stump the eye could be built up and good movement obtained. It had been asked what was the effect of the acrylic prosthesis on the discharging skin-lined sockets. It was inert. In his experience the discharge was unavoidable, whatever sort of prosthesis was worn.

or June of last year he saw a number of persons in this condition among prisoners back from the Philippines. They had a certain amount of blindness and were mentally very dull. Speaking the previous week to the O.C. of the Medical Division, he said that he was not satisfied that anything but the retrobulbar neuritis was an entity; the other things might be hysterical. A medical officer who had been a prisoner of war for three years was of opinion that the whole thing was due to methyl alcohol, which was obtainable in all the prisoner of war camps, and would not have it that these cases were vitamin deficiency at all.

Major A. J. Cameron said that similar cases from the Far East which he had seen seemed to fall into definite groups. The first and smallest was a group in which the pathological findings at the disc were very obvious, visual depression very marked, and an estimation of the visual field only possible by gross confrontation. In the second and by far the largest group there was very little to be seen at the disc and in many cases certainly not more temporal pallor than was frequently found in normal eyes. The visual acuity was not greatly depressed, often being as good as 6/12 or 6/9, but the patient complained of what could be described as "central symptoms". Examination of the field of vision on the perimeter and on the Bjerrum screen showed small scotomata in the paracentral area. In many such cases the scotomata were larger and centro-caecal in type and so much resembled the form of scotoma obtained in that form of chronic retrobulbar neuritis known as tobacco amblyopia that it prompted an inquiry along those lines. He was able to find out that smoking was very prevalent. No tobacco was available from home, and the men smoked what was described as a native leaf. This they all said was stronger than anyone ever smoked in this country. Perhaps that was a factor which should be borne in mind.

The third group was composed of those who exhibited no objective symptoms. The vision was good and their fields were full. It was difficult to decide whether they were functional or were remembering a previous train of symptoms. All these soldiers were well aware of what was meant by vitamin deficiency and they all endeavoured to get their share of rice polishings, red palm oil, grass extract, &c. Notes on production of vitamin preparations in the camp by the prisoners themselves had been furnished to him by Major Burgess, R.A.M.C., formerly of the Malayan Government Medical Service, and Mr. J. H. Piddleston, M.Sc., chemical engineer. These notes were very interesting, but too long to read to the Section. He was indebted to the gentlemen named for the care they had taken in preparing the notes. It was of interest to note that the average duration of "ocular symptoms" was from eight to twelve months, and that many patients found that a return to normal diet and vitamin adjuvants seemed for the time being to exacerbate the visual symptoms. A very frequent symptom was weakness of accommodation.

Mr. F. E. Preston said he had seen a patient who had recently returned to this country. Before the war he had 6/6 vision, and when he saw him his vision was 6/24 in each eye. He diagnosed him as suffering from deficiency disease, but the patient had not complained much about other troubles, he had put down his condition to pure hunger and want of food—he had been fed on rice. The most marked abnormality which he found was his loss of colour sense. He could not do a single one of Ishihara's colour plate tests. He had smoked quite a lot of cigarettes in his hunger—more than he should have done.

Mr. Lindsay Rea said that he could confirm what had been said from the experience of his brother-in-law who had just returned after three and a half years in Japanese hands in Hong Kong. Owing to malnutrition he had suffered from hallucinations of sight such as found in pellagra. A man walking towards him would suddenly appear to throw out his leg sideways like a toy being pulled by a string. This was cured by injections of the vitamin B complex. He was a heavy smoker and got tobacco from the Japanese made from some unknown stuff.

Mr. Lindsay Rea had seen a prisoner-of-war who had been in Germany during the whole of the war. This man, who was in his thirties, had come back with well-marked cataract in each eye of the senile variety; this was progressive. In another man from Sumatra the accommodation had largely failed; his visual acuity was normal. In the cases of non-smokers the retrobulbar neuritis might still be there and might be of the pellagra type but it was as well to inquire what they had been smoking before coming to the conclusion that true retrobulbar neuritis had appeared.

Mr. Affeck Greeves thought that some of these cases might represent something of the nature of toxic amblyopia rather than of retrobulbar neuritis. For example, he had recently seen a man from Guernsey who gave a very accurate description of the symptoms of tobacco amblyopia, and he told him that, in the absence of ordinary tobacco, he had smoked various kinds of dried leaves. The patient's sight recovered completely in spite of the fact that he had resumed the smoking of tobacco as soon as that was obtainable. It was also possible, however, that this type of amblyopia might be the result of malnutrition and not of toxic origin.

Captain E. D. H. Williams, in reply to a member who said that all the cases he had seen had been complicated with malaria, and asked whether that condition was prevalent in the prison camp at Singapore, said that he himself had not had malaria at any time, though he would not like to say what other men got. Malaria was certainly very common in the camp about the end of 1942. In reply to a further question he said that about 1% suffered severe symptoms; they were all under more or less the same conditions.

Fig. 2 shows a zonular fibre becoming continuous with the zonular fibre of the anterior capsule.

This fibre is one of the orbiculo-anterior capsular fibres, the longest and strongest fibres of the zonule. They arise from the pars plana and receive auxiliary fibres along their whole course. They lie in the valleys between the taller ciliary processes, where they form well-marked bundles.

Most of the auxiliary fibres run from behind forwards and inwards, but just behind the posterior ciliary processes they also run from in front backwards and inwards. The zonular fibres here, therefore, have a double attachment which makes for strength and so it is usually just beyond this point that the fibres break.

Are there any equatorial fibres? The answer lies in the development and natural history of the zonule.

(c)



FIG. 1.—Orbiculo-anterior capsular fibres (a); also orbiculo-posterior capsular fibre (b) in close relation with anterior limiting layer of vitreous (c). $\times 250$. Ant. post. section. (Zenker, Mallory's triple stain.)

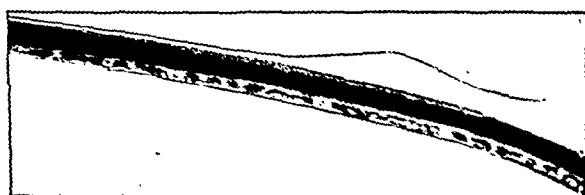


FIG. 2.—Zonular fibre becoming continuous with the zonular fibre of the anterior capsule. $\times 250$. Ant. post. section.

In the embryo and at birth there are a great many more fibres than in the adult. These arise not only from the inner aspect of the ciliary body but from the back of the iris, the angle of the posterior chamber and from the most anterior ciliary process which in the adult lies free from zonular fibres. Also on the lens capsule the space between the anterior and posterior groups of fibres is entirely filled in by equatorial fibres. With age, many of these equatorial fibres disappear and only a few sparse ones or— all may

On the question of glass eyes versus other forms of prosthesis, his own feeling was that one could not really improve upon the best glass eyes. For sockets which were in any way distorted or contracted, a moulded acrylic prosthesis was the only possible answer to-day. Too much attention, he thought, had been paid to the restriction to a limited number of sizes and shapes, in criticizing mass-produced eyes, whether glass or acrylic. The normal socket was such that a limited number of sizes and shapes did give excellent results. If money was no object one could have an individual eye made by an artist for every patient. Nevertheless, the mass-produced eye would serve ordinary purposes.

Squadron Leader Stewart, in reply, said that he had trained one or two people to carry out work on artificial eyes, but whether mechanics would be allowed to take impressions of the socket he could not say; mechanics were definitely barred from taking impressions of the mouth, but whether the socket was considered to be inside the body or not was another question.

One of the speakers had already answered the question about discharge. They were neither better nor worse off by using acrylic; if the glass eye fitted badly there seemed to be more discharge. He did not think this had anything to do with the material itself. He had seen only one or two cases in which a skin flap had been put in, and so far he had not been thrilled with the result.

One speaker had asked about the cost. This was a difficult subject. It was more difficult to make an eye than it was to make a denture. What was the price of a denture? He would have thought it not possible to do anything in the way of an artificial eye in plastic under fifteen guineas. Considerable time had to be spent in taking the impression; it was a skilled operation. Some part of the work could be delegated, but by no means all of it. The work was much more difficult than in the case of a denture and the patient was much more critical.

The material was the same as was used for plastic lenses, but admittedly it was scratchable. The lens could not be rubbed even with fine silk without scratching it. There was a method whereby a slight deposit of glass might be made on the surface to give the necessary hardness, but that was still in the experimental stage. He did not think this trouble, while it arose with plastic lenses, need arise with a plastic eye—he had never seen one scratched yet.

Concerning the question of keeping the socket the right size, he liked to get on to the job as soon as possible after the operation. He had not yet quite made up his mind on the question of whether a socket got small or not. They had had patients who had had the eye taken out as children, and one case he saw about a month ago had never had an eye in. The sooner the prosthesis could be inserted so as to give the right size the better. If one had a socket which was shrunk it was very hard to expand it again.

Some Aspects of the Normal Histology of the Suspensory Ligament of the Lens

By EUGENE WOLFF, F.R.C.S.

THERE is still a great deal of dispute even about the main facts of this difficult subject, and latterly, Duke-Elder bringing it into line with the gel theory of vitreous, has suggested that the fibres of the suspensory ligament are "mainly histological artefact".

First one would draw special attention to the most posterior and innermost fibres of the zonule. These, the orbiculo-posterior capsular fibres (fig. 1) arise from the ora serrata and are inserted together with the vitreous, i.e. with the ligamentum hyaloideo-capsulare of Wieger, into the posterior lens capsule. They are everywhere in close contact, indeed, adherent to the anterior limiting layer of the vitreous. Thus if we detach the vitreous many zonular fibres come away with it; if, however, we merely allow the vitreous to flow away the anterior limiting layer remains attached to the posterior zonular fibres (Garnier). Also this close relation of the zonule to the anterior limiting layer is one of the reasons why there is still no unanimous answer to the question: Is there a hyaloid membrane to the anterior vitreous?

Now the anterior limiting layer of the vitreous is not a hyaloid membrane for a hyaloid membrane must be transparent and homogeneous, and have sharp contours. It has more the structure of connective tissue and shows a striation due to its constituent fibrillae parallel to the surface. It is the close relation of the hyaline zonular fibres which is at any rate partly responsible for the error of calling the anterior limiting layer a hyaloid membrane (see Garnier).

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This fibre is one of the orbiculo-anterior capsular fibres, the longest and strongest fibres of the zonule. They arise from the pars plana and receive auxiliary fibres along their whole course. They lie in the valleys between the taller ciliary processes, where they form well-marked bundles.

Most of the auxiliary fibres run from behind forwards and inwards, but just behind the posterior ciliary processes they also run from in front backwards and inwards. The zonular fibres here, therefore, have a double attachment which makes for strength and so it is usually just beyond this point that the fibres break.

Are there any equatorial fibres? The answer lies in the development and natural history of the zonule.

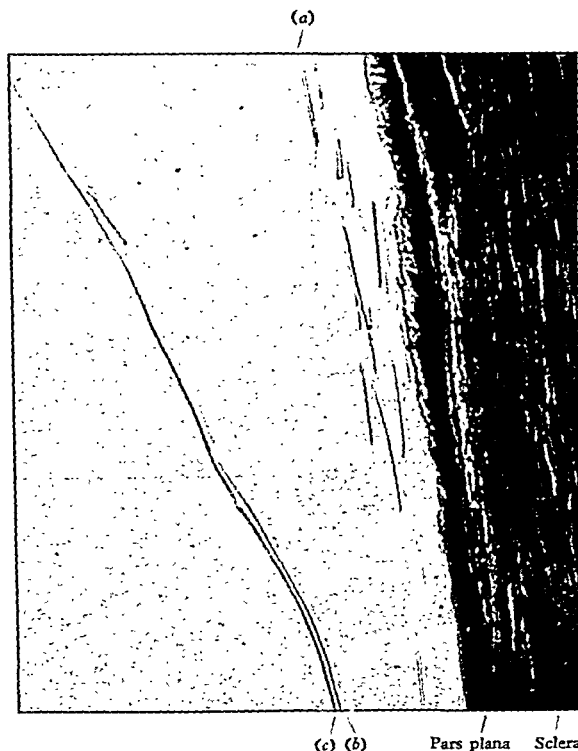


FIG. 1.—Orbiculo-anterior capsular fibres (a); also orbiculo-posterior capsular fibre (b) in close relation with anterior limiting layer of vitreous (c). $\times 250$. Ant. post. section. (Zenker, Mallory's triple stain.)

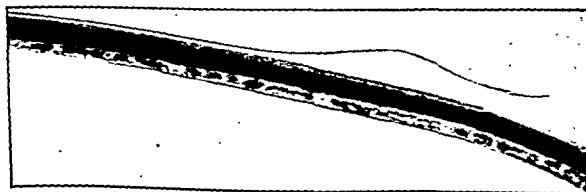


FIG. 2.—Zonular fibre becoming continuous with the zonular fibre of the anterior capsule. $\times 250$. Ant. post. section.

In the embryo and at birth there are a great many more fibres than in the adult. These arise not only from the inner aspect of the ciliary body but from the back of the iris, the angle of the posterior chamber and from the most anterior ciliary process which in the adult lies free from zonular fibres. Also on the lens capsule the space between the anterior and posterior groups of fibres is entirely filled in by equatorial fibres. With age, many of these equatorial fibres disappear and only a few sparse ones or none at all may

remain. The answer then is that equatorial fibres really only exist in youthful eyes (Garnier).

All are agreed that the attachment of the zonular fibres to the ciliary epithelium is very close. Indeed, if they are pulled away some of the epithelium comes away too.

But there is still a great deal of dispute as to the actual method of fixation. Some say that the zonular fibres are processes of the clear cells of the pars ciliaris retinae; others that the fibres can be followed through these cells to the membrane between them and the pigment layer; others again that the attachment is inter-cellular. I would agree with those who hold that the zonular fibres run into the internal limiting membrane of the ciliary body.

I think the colour photomicrograph of a coronal section of the ciliary body stained by Mallory's triple stain shows this quite clearly. (Illustration omitted owing to space shortage.) The blue staining tissue on the inner aspect of the ciliary body is of special interest. Dejean says that this tissue which stains like collagen is already present at the time of the secondary optic vesicle.

If this is true, then the zonule and further back the vitreous cannot be outgrowths from the ciliary epithelium and retina respectively.

As a general rule the various views with regard to the attachment of the zonule reflect the opinions of the authors on its development.

But there is one aspect of the question which has received very little attention. It is quite well known that the normal pigmented epithelium of the ciliary body proliferates, but that the non-pigmented cells can do this is not usually realized. This epithelium may in fact with age form papillary projections which may be placed so close together that the internal limiting membrane between two elevations may appear inter-epithelial. And if a zonular fibre happens to run into the limiting membrane here it would appear as if its origin too were inter-epithelial.



FIG. 3.—Coronal section of ciliary valley. $\times 300$.

Fig. 3 shows some inter-ciliary fibres of which, so far as I am aware, there is no illustration in the literature.

From what has gone before I need hardly say that I believe the fibres of the suspensory ligament of the lens real, very real. Also it is quite clear from fig. 2 that if the zonular fibre be regarded as an artefact then the capsule of the lens must be an artefact too.

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The Nervus Nasalis Complex of Charlin

By MAJOR W. O. G. TAYLOR, R.A.M.C.

Ophthalmic Specialist

THE purpose of this paper is to record in British ophthalmic literature a case of the rather uncommon condition known as the syndrome of the nasal nerve (syn. naso-ciliary nerve) or the nervus nasalis complex of Charlin, and alternative method of treatment.

Case history.—An African soldier in his early twenties was admitted to No. 1 (E.A.) General Hospital on June 15, 1944, with a complaint of pain in his right eye of eight days' duration and unknown cause. On examination the only noteworthy features were blepharospasm and limbal injection; a preliminary diagnosis of iritis was made and the following tests performed:

Conjunctival smear: negative. Kahn test: negative. P.U. smear: no gonococci. Culture: no growth. Urine negative.

Blood-count.—White cells: total 9,400 per c.mm. Differential: Neutros. 37%, eosinos. 3%, lymphos. 52%, monos. 8%.

Treatment.—Ungt. atropinæ 1%, hot spooning, mist. "three fifteens"; each 3 times daily. Four days later it was noticed that beads of sweat gathered on the right side of his nose at the tip, but nowhere else. On wiping them away, they returned within a minute,

and were sharply limited to the terminal distribution of the external cutaneous branch of the right naso-ciliary nerve. The patient stated that this had begun at the same time that his eye began to feel sore.

Slit-lamp examination: Many fine keratic precipitates.

22.6.44: X-ray—sinuses normal.

By July 5, the case had improved so that the sweating was no longer visible, although it could be readily induced in the same distribution by momentary exposure of the face to a radiant heat lamp. At this stage the photograph (fig. 1) was taken.

7.7.44: Slit-lamp examination—K.P. now much larger. Ophthalmoscope—fundus oculi still not visible.

On July 18, the eye was quiet but the vision of the right eye less than 6/60 (V.A.L. 6/6), due to haze of the media. On July 22, there was an acute relapse of both the iritis and the sweating. X-ray examination was repeated and reported as follows:

Major Hopkirk, E.A.A.M.C.: "Ethmoids and sphenoids normal, doubtful opacity of right frontal."

Three days later the eye was worse and the patient complained of pain over the right side of the vertex of the skull and in the right upper teeth. No oedema or proptosis of eye. Two days later—on July 30—there was pyrexia; blood slides were taken for malaria, but were negative. On July 31, the patient complained of a watery discharge from his nose. There was a tenderness on pressure over the right supra-orbital notch.

Dental report by Major E. D. Stanhope (A.D. Corps): "There is no dental cause which might give rise to a reflex pain."

August 12, still complains of pain at inner angle of the right eye and nose, also along zygoma on right side of face. Injection of eye persists. In view of the long persistence of the condition and the lack of any specific indication for treatment it was decided to try the effect of a nerve block. Accordingly 2 c.c. of 3% novotoc were injected at a distance of 2 cm. from the skin, in the middle of the medial wall of the orbit. Three days later it was noted that the eye was much improved, and the patient said it felt better. By August 19 the limbal injection and the sweating were almost gone, and ten days later completely so. He was kept under observation for a further fortnight and then discharged. No recurrence took place.

Literature.—This condition was first described (1930) by Charlin of Santiago, Chile, and elaborated in subsequent papers (1931, 1932, 1936, 1937). The essential features he describes as unilateral rhinitis, pain in the inner angle of the eye, on the side of the tip of the nose and near its root, often accompanied by affection of the anterior part of the eye. "Syndromes frustes" may occur (1931) as is also pointed out by Mangabeira-Albernaz (1939) who believed elevation of ocular tension might occur. Halbron (1936) states that intermediate types make it difficult to distinguish between Charlin's and the "vacuum sinus" syndromes. He explains Charlin's syndrome by a vasodilatation of the anterior ethmoidal artery. The differential diagnosis (from Sluder's syndrome) is discussed by Laskiewicz (1940) and Solonitzky (1936). The aetiological factor is discussed in Charlin's papers—many he thought due to an "épine irritative" in the nose—such as an ethmoiditis, or hypertrophy of the inferior turbinate, stimulation of which caused congestion of the tunnel of the nasal nerve. There were, however, other cases which did not have such a local cause and he found as causes syphilis, diabetes and dental sepsis. The mere performance of the Mantoux test seemed sufficient to cure two cases presumably of allergy to tuberculo-protein.

Treatment was by tamponage of the nose with cocaine and adrenaline (Charlin, Dejean and Artieres, Solonitzky) or directed towards the aetiology in the event of a specific cause being found. The case of Isava (1931) treated by effleurage of a corneal ulcer does not seem to me definitely identified with the syndrome.

Diagnosis.—The differential diagnosis from affections of the pterygo-palatine ganglion may be tabulated thus:

	Syndrome of nasal nerve	Syndrome of pterygo-palatine ganglion
Nasal inflammation	Ant. part inf. concha	Post part middle concha
Relief by coc. and adr.	Applied to ant. part of nasal cavity	Applied to regio gangli. pterygo palat.
Pain	Eye and orbit	Eye and orbit
Anatomical changes	Iritis or keratitis	No anatomical changes in the eye
Hydrophobia	Yes	Yes
Hyperaesthesia and	Cuts of nostrils, forehead and	Not on skin of nose
Herpetic eruption	nose	

DISCUSSION

The anatomical basis of this syndrome is interesting, and can be followed in detail in any textbook of anatomy. Only the most important points are discussed here. The diagram (fig. 2) adapted from Duke-Elder (1932) shows the cutaneous distribution of the terminal branches of the 5th nerve. Areas of pain or tenderness in this case are marked with a cross. From a consideration of the sequence of events it would seem that the naso-ciliary nerve was first involved—branches to the iris and to the skin at the tip of the nose. Under ordinary treatment this improved until on July 22, a relapse occurred, followed by spread of the pain to the scalp (supra-orbital N.), inner canthus (infra-trochlear N.), and right upper teeth (infra-orbital N.). Discharge from the nose was first noted on July 30 and later pain along the zygoma (zygomatico-facial N.).



FIG. 1.

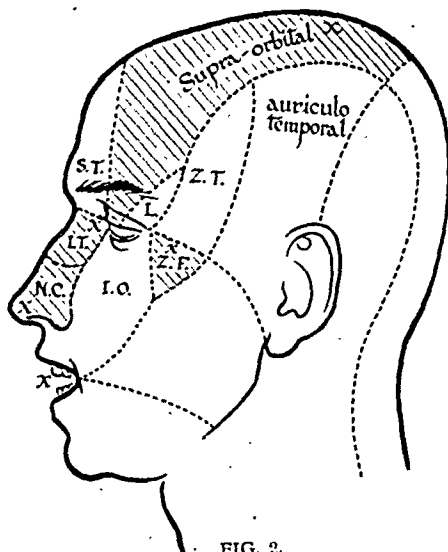


FIG. 2.

FIG. 1.—Photograph of patient showing beads of perspiration on right side of tip of nose and right blepharospasm.
FIG. 2.—Cutaneous distribution of maxillary and ophthalmic divisions of trigeminal (after Zander). Painful spots marked with a cross and affected nervous distributions shaded.

What is the basis of this phenomenon? The autonomic responses of sweating and flushing are presumably axon reflexes (Lewis, 1927). The behaviour of the obscure iritis suggests that it also is of reflex origin, and that somewhere in the pathway of the naso-ciliary nerve lies the cause. It was thought that an ethmoiditis might be the explanation, but in view of the negative X-ray, the rhinologist advised against interference. The frontal sinus is of course supplied by twigs from the supra-orbital nerve, but this did not come into the picture until later. The literature of this condition was not at the time available. However, the theories of Leriche (1939) suggested that blocking of the painful stimuli might bring relief, and an injection of novotox was made over the region of the anterior ethmoidal foramen. This apparently resulted in resolution of the condition in the same period as the cases treated by Charlin (1930) and Solonitzky (1936).

SUMMARY

A case is described of sweating of the tip of the nose associated with iritis and various reflex pains, all strictly unilateral. It is considered that this was a case of Charlin's syndrome, and an alternative form of treatment is described.

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Section of Anæsthetics

President—GEORGE EDWARDS, M.R.C.S., D.A.

[January 4, 1946]

Anæsthesia for Ear, Nose and Throat Surgery.

By WILLIAM W. MUSHIN, M.B., D.A.

EAR, nose and throat operations are made safe or dangerous, easy or difficult, by the anæsthetist. It is a fact that patients still die during and after tonsillectomy from asphyxia caused by a blood clot in the trachea. They die of respiratory obstruction during mastoid operations in a dark theatre. They die of shock and anæmia after laryngectomy, because the surgeon lacked a tranquil, hæmostatic operation area. Yet few of the operations commonly performed in an E.N.T. department should by themselves endanger life.

All the operations performed by the E.N.T. surgeon can be done efficiently under general anæsthesia; and this is the common practice in this country. There is, however, a growing interest in regional anæsthesia for these operations not, as on the Continent forty years ago, because the standard of general anæsthesia was poor, but because it is believed that for certain operations local anæsthesia has virtues not found in any other method. I myself believe this to be so. I feel that E.N.T. operations like those elsewhere in the body fall into three groups. First, those for which local anæsthesia alone cannot be used with complete success. Examples are mastoid operations and, generally speaking, operations on children. In the second group are those operations like tonsillectomy in which the use of a particular method makes little difference to the success of the operation. The patient's wishes are here the determining factor. The last group is a most important one, since it includes not only everyday operations like the Caldwell-Luc, but the more rare life-saving operations like laryngectomy. Here local anæsthesia makes the operation easier and more likely to be successful, and in the case of operations like laryngectomy may affect the chances of survival.

Since both general and local anæsthesia have their place for ear, nose and throat cases, I propose to deal first in general terms with some of the qualities which are possessed by safe and efficient general anæsthesia and then since it is the more novel method in this country, to deal in a little more detail with local anæsthesia.

Safety.—It should hardly be necessary to stress before a Section of Anæsthetics that the patient's life should not be endangered by the anæsthetic. Not so long ago, at a meeting of this Section, it was seriously put forward from the body of the hall that a child of 5, who was to have its tonsils guillotined, should be given a cocktail anæsthetic



FIG. 1.

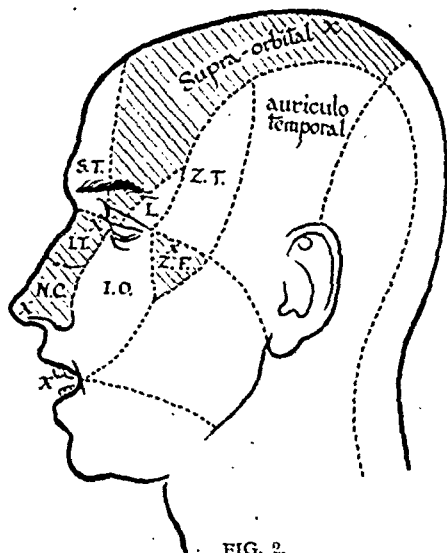


FIG. 2.

FIG. 1.—Photograph of patient showing beads of perspiration on right side of tip of nose and right blepharospasm.
FIG. 2.—Cutaneous distribution of maxillary and ophthalmic divisions of trigeminal (after Zander). Painful spots marked with a cross and affected nervous distributions shaded.

What is the basis of this phenomenon? The autonomic responses of sweating and flushing are presumably axon reflexes (Lewis, 1927). The behaviour of the obscure iritis suggests that it also is of reflex origin, and that somewhere in the pathway of the nasociliary nerve lies the cause. It was thought that an ethmoiditis might be the explanation, but in view of the negative X-ray, the rhinologist advised against interference. The frontal sinus is of course supplied by twigs from the supra-orbital nerve, but this did not come into the picture until later. The literature of this condition was not at the time available. However, the theories of Leriche (1939) suggested that blocking of the painful stimuli might bring relief, and an injection of novotox was made over the region of the anterior ethmoidal foramen. This apparently resulted in resolution of the condition in the same period as the cases treated by Charlin (1930) and Solonitzky (1936).

SUMMARY

A case is described of sweating of the tip of the nose associated with iritis and various reflex pains, all strictly unilateral. It is considered that this was a case of Charlin's syndrome, and an alternative form of treatment is described.

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a diseased internal jugular had just been exposed prior to its ligation. The patient coughed. The vein swelled to the size of a small hen's egg and might have ruptured had not prompt pressure been made by the surgeon.

Hæmostasis.—The E.N.T. surgeon works on tiny structures through small holes. Both the bone he works on and the mucous membrane covering it, are exceptionally vascular. It is no exaggeration that the success or failure of these operations depends very much on whether he can see what he is doing. Even the patient's life may depend on good hæmostasis in the operation wound. I know of patients who have ultimately died because of injury to the dura or lateral sinus lying at the bottom of a mastoid cavity full of blood.

In fact most of the important advances in anæsthesia for E.N.T. operations have been in the direction of making the field of operation more bloodless. Some operations, like the fenestration for otosclerosis, literally cannot be done at all unless the field is virtually dry.

Here are some of the commoner causes which are responsible for a bloody operating field. Their correction is the duty of the anæsthetist: (1) Respiratory obstruction. (2) Straining due to active reflexes. (3) Anoxia. (4) Obstruction to the venous return from the head: (a) tight bands constricting the veins of the neck; (b) faulty position of the head.

The last-mentioned is of particular importance. Good venous drainage of the head and neck cannot take place unless there is an unobstructed venous pathway between the head and the heart. Gravity should be enlisted to help this drainage rather than to hinder it; whenever possible the patient's head should not only be in a natural line with the shoulders but slightly elevated. It may be that the notably dry field obtainable with local anæsthesia for tonsillectomy is partly due to the patient sitting upright. Compare this with the unnaturally extended position of the head commonly adopted for this operation under general anæsthesia. As an example of how the veins of the neck may be constricted, the webbing strap holding the Guy's pattern jack, takes first place.

Prevention of aspiration.—The last of the points bound up with safety is the prevention of aspiration of blood, bits of tonsil or swabs. Under general anæsthesia for operations where this may occur, the airway is kept patent and aspiration prevented by an endotracheal tube; the space between the tube and trachea occluded by a cuff or by gauze packing. Two of the many "don'ts" concerning endotracheal tubes in general are worth repeating here: (1) Don't use a tube unless it is essential; (2) don't use a tube of inadequate bore.

A tube is essential only if without it foreign matter may be inspired or the airway become occluded. To a gathering such as this, this remark savours of the obvious. There is no doubt that endotracheal tubes are often used unnecessarily in this country to the patient's detriment. In my opinion tonsil and mastoid operations in young children do not indicate an endotracheal tube; nor do the majority of mastoid operations in adults. Insufflation of ether vapour into the pharynx is adequate for these operations.

An endotracheal tube has its uses and abuses. Its use for mastoidectomy comes under the latter heading since real indications for this procedure must be few and far between. Apart from the patient with the short fat neck, almost the only justification is an anæsthetist tired at the end of a busy day or one incompetent to maintain an airway by more simple means. I have seen deep anæsthesia induced not for the performance of the operation, but so that an endotracheal tube will be tolerated and this to a patient gravely ill with pneumonia. The fact that most patients survive this insult does not justify its use as a routine.

Using a small endotracheal tube is equivalent to obstructing the patient's airway. Not only is the patient made fatigued and anoxic but the veins of his head become congested, resulting in increased oozing in the wound. If the patient has incipient right-sided heart failure, or the inadequate airway is maintained for a long time, pulmonary oedema may occur.

Following a throat or nose operation under general anæsthesia, the patient is not out of danger until he has recovered his reflexes. The unconscious patient who has just had such an operation needs careful and skilled supervision if he is to avoid grave risk. We are still not free of the tragedy of the patient who is found dead in bed of tonsillectomy. At post-mortem a clot of blood is found obstructing the larynx or bronchi. It is not always possible to send the patient back to bed with active reflexes, and

of rectal avertin, endotracheal tube, nitrous oxide and "puffs of cyclopropane." All this to spare it the ordeal of ether for two minutes. Unfortunately this discussion was never published and this interesting suggestion has not been recorded.

For some years before the war it was common, in anæsthetic literature, to link safety and good results with choice of agent. We have rather preached that safety lies with the anæsthetist and his knowledge of basic principles than on the choice of any particular agent. That this point of view is not confined to the backwaters of the Thames is indicated by the following quotation from a recent paper by Dr. Ralph Waters [1]:

"For each patient who has died from postoperative pneumonia due to irritation of his lungs with the vapor of ether, dozens have died from pneumonia following mechanical obstruction to their air passages. For each patient whose heart has stopped during anæsthesia because of drug effect on the autonomic mechanism which controls it, the hearts of dozens of patients have stopped because the larynx was flooded with vomitus. Perhaps we ought to worry more about the careful supervision of the breathing of our patients and less about our choice of drugs to prevent pain; more about our own personal knowledge and skill with a particular agent or method and less about how someone else says he gets the best results."

Of the general anæsthetic agents, ether is still pre-eminently the one of choice for ear, nose and throat operations—the explosion hazard excepted.

Well-meaning attempts to avoid ether in order to save the patient from theoretical or hypothetical disadvantages of this agent are only made at some cost. For example, nitrous oxide and oxygen, unless reinforced with powerful doses of sedatives, themselves involving some risk of a prolonged depression of the cough reflex, only too often result in a patient who tries to pluck his endotracheal tube out of his nose. If anæsthesia is deepened by reducing the oxygen, we are faced with a patient whose circulation is impeded by asphyxia. The resultant oozing and obscuration of the operative field mitigates against the success of the operation.

Pentothal has but limited use as the main anæsthetic for these operations. It does not as a rule subdue the laryngeal reflexes until it subdues the respiratory ones. Effective cocaineization is necessary, therefore, before intubation or other operations on the larynx can be performed, and cocaine itself is known to be not without its hazards. The prolonged recovery period common after large doses of pentothal, constitutes a greatly increased risk after these operations. Cyclopropane presents the manifold difficulties of maintaining a gas-tight circuit. Trilene is efficient enough but its pharmacology is still being actively investigated and its place in anæsthesia is by no means clear. In my opinion, only when there is danger of explosion and a general anæsthetic is still indicated, should ether be displaced from its premier position as the general anæsthetic for ear, nose and throat operations.

Equipment for resuscitation should always be present and ready for use in an ear, nose and throat theatre, above all places. The two pieces of apparatus I will not do without are a suction apparatus and a means of inflating the patient's lungs. Both of these save lives.

A convenient non-electric portable sucker is that devised by my colleagues Saher and Salt [2]. Any compressed gas can be used with the injector device which entrains air from a bottle connected by tubing to a sucker end. A foot control leaves the anæsthetist's hands free. There are numerous devices by means of which the patient's lungs may be inflated. When these are not to hand, the anæsthetist's own breath blown into his patient's lungs is as good a resuscitant now as it was in biblical times.

Immobility.—Immobility on the part of the patient is essential for safety in E.N.T. operations. I have seen tonsils taken out under gas and oxygen while the patient was struggling, coughing and gagging, and the surgeon's view completely obscured. The danger of aspiration of blood, tonsil or swabs is very great in such a case. In this particular instance, had the anæsthetist but renounced his antagonism to ether, tranquillity could have been achieved at little cost. The patient who strains or coughs raises his intrapulmonary pressure. This is reflected in a rise of pressure in the pulmonary artery, the right side of the heart and the venous system generally. A previously dry operation field becomes filled with blood. I shall have more to say about the undesirability of bleeding during these operations.

I need hardly stress the necessity of immobility during any operation. In delicate operations on the head and neck, a cough may mean a tragedy. I recall a case in which

a diseased internal jugular had just been exposed prior to its ligation. The patient coughed. The vein swelled to the size of a small hen's egg and might have ruptured had not prompt pressure been made by the surgeon.

Hæmostasis.—The E.N.T. surgeon works on tiny structures through small holes. Both the bone he works on and the mucous membrane covering it, are exceptionally vascular. It is no exaggeration that the success or failure of these operations depends very much on whether he can see what he is doing. Even the patient's life may depend on good hæmostasis in the operation wound. I know of patients who have ultimately died because of injury to the dura or lateral sinus lying at the bottom of a mastoid cavity full of blood.

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inadequate nursing supervision, only too common in the present shortage of nurses, exposes the patient to risks of respiratory obstruction, inhaling blood, and even of dying. It is therefore the duty of the anaesthetist to see that nurses or orderlies know how to look after an unconscious patient.

In striving to make anaesthesia for these operations safer, the operating conditions better for the surgeon, and the convalescence quicker and pleasanter for the patient, we have continually asked ourselves the following questions: (1) Is an endotracheal tube essential? (2) Can the operating field be made more bloodless? (3) Can the patient retain his own essential reflexes throughout, so that he can guard himself from the dangers of aspirations? (4) Can the immediate post-operative period be made safer and require little supervision?

The answer to these, we feel, lies in the adoption of local anaesthesia whenever possible.

I would like, here, to pay a tribute to Mr. T. B. Layton, Senior E.N.T. Surgeon at Guy's Hospital for first stimulating me to take an interest in this form of anaesthesia. Local anaesthesia is old, but local anaesthesia without vocal anaesthesia for these operations was something new. I learnt from him two secrets of successful local anaesthesia—the importance of the right atmosphere in the ward and theatre and the importance of gentleness and patience on the part of the anaesthetist and surgeon.

The advantages of local anaesthesia are many, the three main ones in the case of E.N.T. operations undoubtedly being the haemostatic operation area, the immunity from aspiration of blood, and the incomparably pleasanter and trouble-free convalescence. To this I would add one more—the absence of tubes and other foreign bodies in the surgeon's field (I have always winced at the endotracheal tube lying in the cancerous larynx).

I think it would be well at this point if I were to define what I mean by local anaesthesia. I mean perfect and absolute anaesthesia of the whole operation area. I mean an operation by a surgeon who is used to the method and who can operate in silence without strain. I mean a ward and theatre where every doctor, nurse, porter, and even ward maid regards local anaesthesia as a routine method and where every patient feels that whatever form of anaesthesia is used it will be a well-considered choice. He may spontaneously express a wish to be awake or asleep, and if, as I have said, it makes no difference to the surgeon or anaesthetist, his request is indulged. Other patients are not questioned regarding anaesthesia, thereby avoiding the embarrassing necessity on the part of the patient of making a decision without the knowledge on which to base it. Should the anaesthetist decide on local anaesthesia, no apologetic explanations are made to the patient since none are needed. Any disparaging reference to local anaesthesia in the patient's hearing undermines his confidence in the method without which the smooth course of the anaesthetic is jeopardized. A visit to a centre where the advantages of local anaesthesia are exploited will convince one that mere technique is not enough; the correct atmosphere is essential. The substitution of nerve blocks for inhalation anaesthesia, by itself will not bring success.

In this general review I have neither the desire nor the time to describe the technical details of all the blocks used for E.N.T. surgery. I propose to outline briefly the method as used for two typical operations, one on the maxillary antrum and the other on the larynx. My intention is to demonstrate that the blocks are not difficult if they are backed by a knowledge of the relevant anatomy. I personally consider it a waste of time to try to teach local anaesthesia unless the anatomical details are thoroughly understood and can be visualized by the student. The proper place to learn local anaesthesia technique is not in the lecture room but in the post-mortem room, and later in the operating theatre, with the guidance of an experienced anaesthetist.

With regard to premedication before local anaesthesia, my only comment here is that when the confident patient is in the hands of the expert anaesthetist—common enough after all in dental practice—he should need little or none. Gentleness and consideration are more important than morphia, although this drug should be used as freely as the patient's and the surgeon's temperament demand.

Here followed brief descriptions of the technique and results of bilateral vagus nerve block and maxillary nerve block. Vagus nerve block for major laryngeal and oesophageal surgery has already been described in the *Proceedings* [3].

Maxillary nerve block is produced by passing a needle through the skin of the face in front of the ramus of the mandible and below the zygoma into the sphenopalatine fossa. Injection here produces anæsthesia of the maxillary nerve and the sphenopalatine ganglion and their branches.

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Mr. R. G. Macbeth: The operative techniques of otolaryngology are not necessarily the most difficult, but because many of them involve the vital airways, they call for special methods. Similarly, because the surgeon and anæsthetist are both claiming those airways, the anæsthesia presents special difficulties. Unless both parties are reasonably skilled, each may hamper the activities of the other. I believe that the operations of my specialty offer the general anæsthetist some of his greatest difficulties; and conversely, if the anæsthetist is less than expert, the surgeon carries out his share of the work less than well.

On the continent of Europe methods employing local and regional anæsthesia are most usual even for mastoid surgery, and it is only now that there is a realization that skilled general anæsthesia is sometimes a help to the surgeon. It is astonishing to our eyes to find an article in a recent Scandinavian journal in which the author triumphantly describes 500 tonsillectomies under general anæsthesia. The anæsthetic method noted and the apparatus illustrated would not commend themselves to you as very advanced, but the continental trend towards general anæsthesia, and the British trend towards regional, surely represent two facets of the same mental attitude, namely a healthy dissatisfaction with the *status quo*.

The popularity of general anæsthesia for E.N.T. operations in Great Britain is probably not unconnected with the facts that this country is the birthplace of practical general anæsthesia, and that the specialists in this field have for many years been really skilled. In 1936 there was a combined meeting of this Section with that of Laryngology. At that meeting an eminent anæsthetist, noted for his skill at endotracheal work announced that if he were having his tonsils removed again, he would choose a local anæsthetic. It was there, too, that Mr. Layton enunciated "the principle of the guarded larynx". He emphasized that this is the keystone of the edifice of safety and success in this work. While accepting that principle, I would agree with Dr. Mushin in going a long way further than that in my interpretation of the contribution I would expect of the anæsthetist to the whole of the operation.

I am completely in agreement that the anæsthetist can and should take a big share in the achievement of immobility and of hæmostasis. (What a joy to the ear of the otolaryngologist it is to hear an anæsthetist confess that anoxia tends to produce oozing, rather than proclaim loftily that I am merely noticing the blood more because it is dark in colour!) I share his view, too, about tubes placed unnecessarily in the larynx of anybody, and especially in that of a child. Jackson has taught us that the sub-glottic cellular tissues of children are particularly easily injured. His dictum that a rigid or semi-rigid tube should remain in a child's larynx for the shortest possible time, deserves the greatest respect. Again, the patient with acute mastoiditis usually has a concomitant upper and lower respiratory infection and in such circumstances a tube passed into the larynx and trachea is likely to lead to trouble below the cords.

I also wish to break a lance in condemnation of pentothal, where this is used as the sole anæsthetic agent in nose and throat operations. If you give enough to get all the relaxation we may need, I am convinced that recovery may be delayed, and aspiration becomes a real danger. If you use local anæsthesia and give the patient just enough pentothal to make him drowsy, I have no quarrel with that; but I am most distrustful when a small nose or throat operation is proposed and somebody says: "All we want is a few cubic centimetres of pentothal". I have said it myself before now, and it has not worked.

I take the view that whether the anæsthesia be general or local, it is the job of the anæsthetist to induce it and to maintain it. The method to be employed in any one case should not be dictated by either of us singly, and least of all by the patient; but any of the three parties should be ready to compromise to suit particular circumstances.

As a pupil of V. E. Negus, I was early introduced to the value of local anæsthesia in some operations on adults. But it does demand of the anæsthetist familiarity with the anatomy of the parts to be prepared for operation.

There are two more advantages of local anæsthesia in otolaryngology: (1) It puts a premium upon gentle and precise operating, and therefore stimulates a good technique. (2) The operating time is shortened remarkably because of the diminished oozing, that bugbear of the otolaryngologist. In this connexion I am not pleading that speed of operating is an end in itself, but other things being equal, it is surely an advantage.

It has been stressed that a quiet and orderly environment is essential. If the surgeon is a querulous type, who habitually has his whole theatre staff in a state of nervous tension, or one who gives way to sudden bursts of vocal violence, the patient had better have a general anæsthetic.

Premedication.—If the part has been properly anæsthetized then the operation is painless, and I deprecate whole-heartedly the giving of large quantities of morphia to cover up deficiencies of technique. But I think that enough premedication should be given to blunt the minor discomfort of the application of the local anæsthetic, to allay the patient's natural apprehension, and to diminish his appreciation of the incidental discomforts inseparable from lying or sitting on an operating table. After all the patient's environment lies partly within himself.

I prefer local anæsthesia in the nose and throat operations I am called upon to do, mainly because at all stages the patients are physically so well. It is common, I find, for patients who have had a tonsillectomy or a Caldwell-Luc operation under local anæsthesia, to start reading a novel on their return to bed, and usual for them to take a full meal two to three hours later. These people are not called upon to recover from the intoxication of a general anæsthetic (at best a bad hang-over), nor from the gastro-enteritis due to much swallowed blood; so that their recuperation is accelerated and they are fit to leave hospital several days sooner than they would after the same operation performed under general anæsthesia.

Patients often dread not the operation but the anæsthetic; and how relieved they often are to learn that they need not be put to sleep. If any of our own nurses or students need a tonsillectomy we find that about 75% choose a local rather than a general anæsthetic. These people have mostly seen the operation done under both methods and their choice is, I feel, significant.

Dr. Mushin has made special reference to the Caldwell-Luc type of antrostomy and to laryngectomy. Many surgeons now think the former a better operation than the simple intranasal antrostomy in most cases, and consequently anæsthetists will encounter it more often. I would strongly commend the method described by the reader. If it be objected that the use of a hammer and chisel by the surgeon must be very unpleasant for the conscious patient, I would agree; and hasten to add that the use of a dental burr obviates this.

Various technical factors have made laryngectomy an operation which can now be recommended in the confidence that the outcome is likely to be successful; whereas a few years ago that operation had a mortality rate of about 30% in the best hands. Among the factors which have contributed to this pleasing state of affairs, I would place regional anæsthesia very high, and the vagal block has put a polish and smoothness upon the technique which it previously lacked. This is a lengthy operation and when regional block is used, the lack of surgical shock is most striking. I believe that the interruption of the very rich sensory nerve supply achieved by the anæsthetist's needle is largely responsible for this. When general methods are used, either the patient is kept at a deep level throughout or, if he is run light, too many strong afferent impulses get through to the higher centres. Although Crile's theory of shock has been considerably discredited, I feel sure that in the neck, powerful sensory stimuli are best eliminated.

In conclusion, I would say that while I am not fanatically advocating a local technique wherever possible in otolaryngology, the method should be given a fair trial.

Mr. T. B. Layton recounted three of his experiences.

(1) The first was of Professor Hajek in Vienna in 1912. It was remarkable that except for two new principles subsequently introduced there is but little change in technique since that day.

He did his first maxillary sinus operation under local anæsthesia successfully in November 1912. Two attempts at that date at tonsillectomy were not so successful. In one he took them out from a contemporary fellow-student. They came out but the doctor still refers to it when they meet. The other was a partial success, for though only one tonsil came painfully out the student, who was the patient, married the nurse who squeezed his hand.

(2) The second experience was the visit of Dr. Graham Brown of Brisbane to England in 1923, who taught him to inject the second division of the 5th nerve through the mouth, an approach that he had since thought far better than those through the orbit or cheek, but the one described by Dr. Mushin to-day was new to him. It looked very good except that personally he found himself unable to do any of those injections, at which others were so skilled, that involved striking a bit of the bone with the needle, withdrawing it and pushing it forward again in an altered direction. It was Mr. Graham Brown's insistence that encouraged him to stick to local anæsthesia and to persist in the injections.

(3) The third experience was a visit to Amsterdam in 1928 when the visiting association saw Professor Noordenbos remove a larynx under local anæsthesia and he spent a morning watching the Professor do general surgery under the approach that everything should be done under local anæsthesia unless there were some special reason against it. He then became convinced that whatever might be true of the body generally this was the future of nasal surgery.

Professor Noordenbos summed up local anæsthesia by saying: "It is kinder to the patient; but a greater strain upon the surgeon and therefore more worth doing." From this quiet remark arose his present conviction that in operating under local anæsthesia

it is the mental factor rather than the physiological or anatomical that holds first importance. Every stimulus to the thalamus by whatever route from below or from above must be eliminated or reduced to a minimum to gain success.

The idea introduces a new approach to operative surgery. It makes the theatre technique as important as the surgical technique. It will make a similar change in hospital construction. The hospitals throughout the land that those now back from the war will build will need their theatres in a quiet corner of the hospital with padded ceilings, floors and walls so that no sound from without can reach them, and then those within will gain full benefit from this technique which entails not a sound arising within the theatre except the quiet firm voice of the surgeon encouraging the patient and warning him that he is going to do something that will be uncomfortable. This form of "vocal anaesthesia" is an essential part of the technique.

Dr. H. W. Loftus Dale: I have proved the efficacy of the block of the 2nd division of the 5th nerve and the sphenopalatine ganglion in a series of 300 cases, most of which were for Norman Patterson's radical sinus operation and Caldwell-Luc's, using, however, a different approach (see *Proc. R. Soc. Med.*, 1945, 38, 624-626). I can confirm the value of the technique.

I have also used the bilateral vagal block and have been greatly impressed by the complete absence of all respiratory tract reflexes. A marked rise in pulse-rate (70-140) sustained for ten to fifteen minutes was observed. One patient having a bronchoscopy for ? carcinoma of lung complained afterwards of the very unpleasant sensation of not knowing he was breathing, save by hearing his respirations passing through the bronchoscope.

What is the best anaesthetic for bronchoscopy in small children?

Nitrous oxide is inadequate, ether excluded owing to explosion risks, the danger associated with the use of small electric bulbs having been stressed by experts at a meeting of this Section. Trilene cannot be counted on to provide the necessary relaxation and though the number of administrations up to date indicate a much less chance of primary cardiac failure, this risk cannot entirely be excluded.

The dangers of chloroform are accentuated in bronchoscopy since there is the chance of vagal inhibition or ventricular fibrillation due to sympathetic stimulation. It has been pointed out that stimulation of the stellate ganglion in cats under chloroform anaesthesia produces ventricular fibrillations more readily than does injection of adrenaline. I have had some anxiety more than once, notably a case of cardiac arrest after the successful removal of a halfpenny from a small child by means of a coin catcher, which, happily, responded to somewhat energetic restorative measures including inversion.

And children are said to be supersensitive to cocaine.

Mr. A. B. Alexander: W. W. Mushin considers a mastoid operation unsuitable for local anaesthesia. While it is admittedly preferable to perform mastoid operations under general anaesthesia in the majority of cases, the local technique is nevertheless existent and important, and the now revived operation of "fenestration" brings this technique again into the limelight. The impact of the gouge is often unpleasantly felt—a point which Dr. Mushin stressed with regard to the Caldwell-Luc operation—and I have found it useful, and relieving to the patient, to place a piece of thick rubber tubing in the patient's mouth and when using the gouge and hammer to ask him to bite on it firmly.

W. W. Mushin condemns the small bore tube: I find it a useful implement of anaesthesia for the removal of polypi from the cords: its size enables the surgeon to displace it, and to enjoy a free field of operation while at the same time gaining the advantages of an intratracheal, unhurried and well-maintained anaesthetic. The airway is assured by the introduction of the laryngoscope, and I would like to ask Dr. Mushin whether he does not regard this type of anaesthetic as safe, and as worth while continuing.

The regional anaesthesia for the Caldwell-Luc type of operation by nerve block is, in my view, open to one major criticism: i.e. that it is quite unnecessary. Regional anaesthesia does not exempt the surgeon from procuring surface anaesthesia of the nose in addition. This, as Dr. Mushin has pointed out, is due to the fact that not only the second branch of the trigeminal nerve provides sensory innervation of the nasal mucous membrane. Surface anaesthesia of the nose, augmented by novocain infiltration of the canine fossa and surface anaesthesia of the mucous membrane lining the antrum is, by itself, sufficient for the Caldwell-Luc type of operation, and the regional block, while doubtless an impressive performance, can easily be dispensed with.

Premedication I consider to be of great importance in local anaesthesia. I have learnt the value of premedication from Mr. Layton, and would not now care to perform an operation under local anaesthesia without it. In the surgery of the antrum it enables one to keep the patient in a twilight sleep throughout the operation.

As for tonsillectomy under local anaesthesia: during the war I operated on a large number of sailors at the Southern (E.M.S.) Hospital. An Admiralty ruling existed, whereby no sailor was to be made to undergo an operation under local anaesthesia unless he had out of every 10 patients expressed a predilection for local anaesthesia. 4 out of every 10 could, after initial hesitation, be persuaded to have the operation done under local

anæsthesia. The remaining 50% preferred a general anæsthetic under all circumstances. These figures, while different from Mr. Macbeth's, may give a clue as to the proportion of patients we can expect to operate on under local anæsthesia amongst groups of people not attached to a hospital.

Dr. R. W. Cope: The anæsthetic technique for the operation of removal of tonsils and adenoids in children at the Hospital for Sick Children, Gt. Ormond Street is as follows:

The principle of the method has not altered at all since Waugh introduced his operation in 1907. Waugh dissected the tonsils and curetted the adenoids under very deep anæsthesia, which was produced originally by chloroform. The main points of the operation which concern the anæsthetist are these: a small sandbag is placed under the child's shoulders and the head is fully extended so that the occiput only rests on the operating table. The mouth is kept open by the use of Waugh's gag and the tongue is pulled firmly and continuously out of the mouth by an assistant holding a pair of tongue forceps of the Mayo towel clip pattern. These forceps take a good bite of the tongue at least 1 cm. away from the tip. If they are placed in this position then the tongue will suffer no trauma at all, however long the forceps are left in position. The other duty of the assistant's hand which is holding these forceps, is to push upwards, that is, towards the surgeon, on the point of the chin. Failure to do this simple act causes a greater or lesser degree of respiratory obstruction immediately. No Boyle Davis gag is used, and this fact coupled with the deep plane of anæsthesia allows the faucial pillars to be perfectly relaxed throughout the operation.

The anæsthetic vapour, whether it be carried by air from a foot-bellows or by oxygen from a cylinder is insufflated into the mouth by means of a "J"-shaped metal tube. This tube is weighted in its vertical part, while the opposite end curves over the teeth and lies just inside the mouth cavity.

For many years pure chloroform was the anæsthetic agent used, later a change was made to ether and air; now oxygen is used in all the theatres as the vehicle carrying the ether vapour.

Premedication has been used for over twenty-five years. This is just as important as the anæsthetic itself, certainly in the case of children to abolish their natural fears of the mask being put on their faces. By his perseverance and teaching of the importance of this subject, Sington, a late President of this Section, instituted a routine use of paraldehyde *per rectum* for these and other cases. This practice was most gladly welcomed by the patients and the anæsthetist, and held a well-deserved popularity for many years. But now the method for producing the same state of quiet sleep has changed, and some form of oral barbiturate has taken the place of paraldehyde. At the present time nembutal 0.6 grain per stone of body-weight seems the most popular drug, although just before the war I was using secconal 0.75 grain per stone with what I thought were better results than with the former preparation.

The foregoing remarks briefly show how little this particular operation and anæsthetic technique has changed since its introduction so many years ago. At the present time I am told it is carried out an average of 35 times each week at Gt. Ormond Street.

Section of Otology

President—A. J. WRIGHT, F.R.C.S.

[November 2, 1945]

Cochlear Deafness¹

PRESIDENT'S ADDRESS

By A. J. WRIGHT, F.R.C.S.(Bristol).

As a result of clinical and pathological research carried out during the last ten years many of us have come to regard Ménière's disease as an entity. It is common ground that the auditory disturbance in the form of deafness, tinnitus or both precedes the vertigo in the majority of cases and often by a long period. We therefore must arrive at the conclusion that we otologists see a large number of cases of perceptive deafness without vertigo which nevertheless belong to the entity of Ménière's disease. I think there is also little doubt that this group of cases of perceptive deafness includes the majority of those the nature of which has been uncertain in the past.

In 1937 I read a paper before this Section under the title of Aural Vertigo in which was included a summary of what seemed to me to be the clinical picture of the cochlear element of Ménière's disease (Wright, 1937). Since that date similar clinical findings have also been published, notably by Crowe (1938), Cawthorne, Fitzgerald and Hallpike (1942) and Altmann and Fowler (1943). In all these descriptions, however, the auditory picture has been included as part of, and rather overshadowed by, the vestibular element.

I feel therefore that I might possibly make a useful contribution to-day by endeavouring to draw a more detailed picture of this disease as we see it in the absence of vertigo.

An additional reason for making this attempt is that avoidable errors in diagnosis are not uncommon. Thus I find that many cases referred to me have been previously treated as cases of middle-ear defect with repeated inflation, &c. The reason for this is understandable in that superficially the picture presented does suggest a derangement of the middle ear.

I propose to deal with each symptom in turn and then briefly bring these together into one picture:

Sex and age.—There is no significant incidence in regard to either sex. While this type of cochlear deafness is most commonly met with in adult life cases occasionally occur in children.

Onset.—The earliest symptom complained of is usually tinnitus and this may exist for some considerable period before any appreciable defect in hearing is noticed.

Sometimes the history is given of a dramatically sudden onset with deafness and tinnitus both of which may be of high degree. Such an onset may be described as being accompanied by the sensation of a blow on the side of the head or of a loud bang in the ear. This occurrence would seem to suggest a vascular origin, such as a hæmorrhage but from a careful consideration of the subsequent course of the complaint, in which a rapid return of the hearing may be noted, I am satisfied that these cases do conform to the usual picture.

¹ Under a grant from the Nuffield Trust.

anæsthesia. The remaining 50% preferred a general anæsthetic under all circumstances. These figures, while different from Mr. Macbeth's, may give a clue as to the proportion of patients we can expect to operate on under local anæsthesia amongst groups of people not attached to a hospital.

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Premedication has been used for over twenty-five years. This is just as important as the anæsthetic itself, certainly in the case of children to abolish their natural fears of the mask being put on their faces. By his perseverance and teaching of the importance of this subject, *Sington*, a late President of this Section, instituted a routine use of paraldehyde *per rectum* for these and other cases. This practice was most gladly welcomed by the patients and the anæsthetist, and held a well-deserved popularity for many years. But now the method for producing the same state of quiet sleep has changed, and some form of oral barbiturate has taken the place of paraldehyde. At the present time nembufal 0.6 grain per stone of body-weight seems the most popular drug, although just before the war I was using secconal 0.75 grain per stone with what I thought were better results than with the former preparation.

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Hyperacusis.—I have on one occasion recorded what was apparently a true hyperacusis early in the disease, i.e. an audiogram curve above the normal level from an ear in which there was a complaint of tinnitus and hypersensitiveness. More frequently the complaint is of the unpleasantness or even pain associated with loud sounds. Such sensitiveness is found both in the early and late stages of the disease. Thus the patient, although very deaf, may complain bitterly of the discomfort produced by speech when loud enough to be audible.

Tinnitus.—This is the most constant symptom and not infrequently the earliest. It was absent, in my experience, in only 4% of cases but these were otherwise typical. Its most striking characteristic as met with in this disease is its variability both in type and intensity. It also shows the same variability in degree as do the deafness and other symptoms. I find in my records some twenty different types described by the patient. Apart from whistling, hissing, buzzing, the noise of machinery and throbbing which form the most common types, the sound of a bubble bursting, a clicking on movement of the head and a buzzing brought on by noise only are noteworthy. I think it is probably in this disease that we meet with the nearest approach to an intolerable tinnitus.

Membrane and middle ear.—In my previous series, some 20% showed old changes in the tympanic membrane or middle ear consisting of scarring, opacity or retraction. In this further series, the figures are almost precisely the same, and, as has already been said, this proportion is such as one finds in cases seen for infection in nose, mouth or throat, but without any labyrinthine disease. Apart from the question of gross disease of the middle ear, I have noted on several occasions the existence of a dilated vessel down the handle of the malleus, and, on one or two occasions, a blush due to hyperæmia of the inner tympanic wall such as one is wont to associate with otosclerosis. I suggest that these findings are not inconsistent with a labyrinthine congestion, and I have been interested to note that Monteiro (1938) has recently recorded the dilatation of this vessel in cases complaining of tinnitus and swimmy sensations in the head.

SUMMARY

The cochlear lesion of Ménière's disease precedes the vestibular in the majority of cases and often for a long period. The clinical picture thus presented is of tinnitus variable in type and degree, with progressive deafness which is usually unilateral. The deafness tends to be variable and is often accompanied by hyperacusis and paracusis. It is perceptive in type but tuning-fork tests are liable to mislead if masking of the better ear is not employed. A sense of fullness in the affected ear is usual and inflation may produce a short-lived improvement in the hearing. These latter findings tend to lead to a mistaken diagnosis of a middle-ear defect.

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Mr. F. W. Watkyn-Thomas said that the President deserved thanks for giving an extraordinarily clear picture of a most difficult problem. He found himself, however, in disagreement on certain points. First of all as to the points on which he agreed; he was most grateful for the President's reminder as to the confusion of diagnosis between middle ear and cochlea. Although it had been emphasized abroad, it was still not sufficiently widely recognized in this country that with a perfectly straightforward middle-ear case, such as a blocked Eustachian tube and an impressed membrane, one could get a loss of bone conduction.

On the question of septic foci he had not been very fortunate in his results, but where a septic focus was responsible for a nerve deafness, the removal of that septic focus was a "dramatic success"—but it was either nothing or everything. Curiously enough, he still had to say that his best results had been in cases where the septic focus was dental or abdominal, such as the gall-bladder. He had now seen three dramatic cures of an apparent early Ménière's as the result of a cholecystectomy.

Among the present causes of nerve deafness he was wondering whether they should not include an over-enthusiasm for sulphonamide dosage. It seemed to him that he had seen an increasing number of cases lately, and some of them bore out that suggestion; he quite admitted the possible alternative—in each case the deafness might have been due to the toxic process. In the case of an old lady with general peritonitis who had had a long course of sulphonamide treatment and who showed an enormous increase in her deafness, a pure nerve deafness, it could be said, he thought, with justice, that the increased deafness had nothing to do with the sulphonamides, it had to do with the lowering of resistance and the septic absorption. But this was a thing to remember.

The point on which he was in disagreement with the President was the vascular element in some of these cases. He quite agreed that a large hæmorrhage would be irrecoverable,

Such an occurrence should be expected in that the vestibular symptoms frequently present a similar dramatic onset and resolution. I find that I have noted such a type of onset in some 7% of cases.

A history of trauma as the exciting cause is frequent, as examples of which I would instance the explosion of a firework in a confined space or the exposure of the side of the head to a cold draught during a long motor drive.

Instead of, or in addition to, tinnitus and/or deafness some form of paracusis may be the earliest symptom. On more than one occasion patients have come to me complaining simply of an altered pitch perception in one ear, usually in the high tones. Such a defect, as one would expect, is more likely to be noticed by an individual with a trained musical ear.

Hyperacusis in the form of discomfort in the ear produced by any loud sound is sometimes an initial symptom; but in my experience tinnitus usually accompanies this.

Hearing loss.—The degree of defect ranges from one which is only discovered as a result of careful testing down to a total loss. From the patient's standpoint the deafness is most frequently unilateral although careful testing will often discover a defect in what the patient regards as a perfect ear.

From a clinical standpoint Ménière's disease does not frequently produce a high-grade deafness in both ears—my records showing a figure of 8% in this respect. When it does so it is usually in cases in which the deafness was definitely bilateral in onset. Where the complaint is decidedly unilateral in degree there is a strong probability that the other ear will retain useful hearing in the future.

Type of hearing loss.—This is perceptive but if care be not taken in the interpretation of tuning-fork tests a mistaken diagnosis of a conductive deafness may be made. It must of course be recognized that the cochlear lesion may occur in an ear already the seat of a conductive defect and therefore presenting a mixed type of deafness. Such cases usually present gross evidence of middle-ear abnormality on otoscopy.

Tone loss.—The most usual finding in the early stages is a high tone loss. Later all tones are involved. Occasionally the audiogram presents a spiky picture and an early low tone loss is also sometimes found. There is therefore no typical audiogram in Ménière's disease.

Tuning-fork tests.—Unless these are used with the utmost care they are liable to lead us astray. With a unilateral deafness of pronounced degree Rinne and bone conduction tests will inevitably mislead in the absence of masking of the good ear.

Weber's test may not so frequently lead to error.

Thus I find that I have recorded in some 4% of cases a reference of the fork to the affected ear and in such cases you will sometimes find that the side of reference will vary with the pitch of the fork concerned. The false result in such cases is, I suggest, perhaps due to the abnormality of the sensation produced in the diseased cochlea.

Paracusis.—This is a frequent and often an early symptom but may persist to a late stage when there exists a gross hearing defect. It is most often described as a general distortion and jangling of sounds heard but as already stated may present an orderly picture in which to one of musical ear it is noted that musical notes are sharp or flat as the case may be. Such a change in pitch perception seems to occur at the margin of a tone defect when present. I have noted six cases in which such a condition was investigated in some detail. In these I was interested to find that in all altered pitch perception in high tones was always sharp and in low tones always flat. Two of the six cases presented an altered perception at both the upper and lower ends of the scale and in these also the high tone was sharp and the low tone flat. If this should prove to be a constant observation interesting deductions might be made as to the responsible cochlear change. There would seem to be possibilities of alterations in length, tension and loading in the basilar membrane or other vibrating structure.

Variability in hearing is very frequent and one of the most dramatic features of the disease. Periods of deafness often come on rapidly and disappear as quickly, any associated symptom such as tinnitus often following the same course. So common and suggestive is this variability that I am in the habit of inquiring for it early in the taking of a history. Its presence to a pronounced degree is almost diagnostic.

Sensory phenomena.—The great majority of cases complain of a fullness, numbness or feeling of pressure in the ear. This may sometimes amount to a sensation of pain in the ear or over the mastoid. There may often be headache which may be frontal, occipital, or temporal or even be described as radiating down the neck. Occasionally a sensation of something loose in the ear on movement of the head is noted.

of the ear in these cases must act during the period when the vestibular apparatus had already been formed but the cochlear apparatus had not yet been developed.

There was one annotation to be made. Everybody, he was sure, had seen cases of typical Ménière's disease or attacks in which no disturbance of hearing occurred. These cases were rare, but they did exist. In such cases it was necessary to conclude that this was a different sort of Ménière's as compared with ordinary cases.

He thought also that it would be highly desirable if somebody interested would survey again the whole of the tuning-fork tests in view of the present possibilities of improved acoustic methods. The tuning-fork tests were still based on statements and findings which were made more than sixty years ago. The original Weber test was not really meant as a test. What Weber did was to note the fact that if the tuning-fork was put in the middle line of the skull and one ear closed with the finger, the sound of the note was perceived in the closed ear. The Weber test as well as the Rinne test well deserved to be examined more closely, because no one, so far as he knew, was aware of what difference in hearing power between the two ears must exist in order to produce a Weber result. On the other hand, it might possibly be that the Weber test was so fine a test that it showed lateralization in the cases where no other means of testing the hearing showed anything to be wrong.

As regards Mr. Cawthorne's comments on the Rinne test, he had always been of opinion that in cases with more than a certain amount of hearing defect the Rinne test became unreliable. Not everything was quite clear as yet about the Rinne test. When they began to undertake surgical destruction of the whole labyrinth they found that afterwards, when everything was healed, in many of these cases, with one destroyed labyrinth, the tuning fork was referred to the operated side. There must be something in the acoustic conditions of the bony skull which furnished the reason for this, but as yet it was not understood. The President's explanations, valuable in themselves, might induce further study.

Mr. Ian Robin asked how long one waited in a case of unilateral deafness and tinnitus, before vertigo arose, while making a diagnosis of Ménière's disease. Was it necessary to have tinnitus to diagnose Ménière's? If there were deafness and vertigo without tinnitus could that be put down as Ménière's?

The President, in reply, said that he had intended to present quite a simple little picture of one facet in this very involved and complicated disease. They had described cases of Eustachian obstruction with perceptive deafness, treated them, and all the deafness disappeared. How common was that? So many individuals had said that it occurred that he must accept it, but how often did it occur? He thought it was very rare.

He could not see any reason why there should not be hæmorrhages in the cochlea and thrombosis in a vessel; it would seem inevitable. Twenty years ago he used to write to the doctor and say that that was what he expected had happened, but he thought personally that the general picture showed that the vascular element was not the usual one.

He, the President, thought that Mr. Vlasto had experienced the same condition in a minor degree. When these conditions started in a minor degree they usually remained so, and in Mr. Vlasto's position, if his pipe were a great joy to him, he would continue with it. On the other hand, if there were any dead teeth he should have them out. The "Punch and Judy" sound was quite typical. That type of distortion was the sort of thing that patients told one about, and it was probably diagnostic, and was found only in this type of cochlear deafness.

The President, continuing, said that the prognosis was particularly good, especially in a mild condition which remained mild.

On the question of injury as the first step in a progressive change in the labyrinth he could not tell how often a progressive lesion was found following an injury. He saw a lot of cases with progressive changes in the labyrinth, and in a few of these there was a history of injury.

In reply to Mr. Forster, he had always found that general picture of interstitial œdema and so on rather vague. He remembered that at Copenhagen several patients were shown with classical Ménière's disease and various things were picked out and they were asked whether they were not all abnormal. Frankly he did not think so. He thought the evidence that reducing people's fluid intake did diminish the severity of their symptoms was fairly established. A large number of intelligent observers had produced evidence to that effect. But it had its risks. He saw a man in a nursing home who was getting renal colic because of oxaluria and he had oxaluria because he had Ménière's disease and had stopped drinking; he had been drinking only small quantities for some years. He advised him to drink and to have his teeth out.

On the question of the motor-car and the vertiginous driver, it was hard to say how big was the risk. Probably it varied in each case. His experience had been that there was practically always enough warning to enable the driver to run on to the side of the road and put on the brakes. But there was a very serious legal position over certification, and if the question was put as to whether attacks of giddiness were experienced, it was necessary to say that they must not drive a car. Apart from the legal question, he did not believe that the risk of accident resulting from an attack of vertigo was a very serious one.

He had been asked how long one should wait in a case of defective hearing before deciding that the defect was due to the condition they had been calling Ménière's disease. He would not wait at all. His object had been to present a plea that this could be recognized at the beginning, that one did not have to wait for vertigo, which might never happen, but that the auditory picture was the same one in this stage as it was in the established condition.

but the question of—he did not know whether the phrase was legitimate—an exudative hæmorrhage must be taken into account—the sort of thing one saw occasionally in the terminal branches of a retinal vessel where there was a certain degree of retinitis and apparently some localized hæmorrhage. He had himself noticed this “come and go” of symptoms in some of these cases, but they had not ended up as Ménière's condition, they had ended up in a severe degree of perceptive deafness.

He agreed with the President as to the absence of any typical audiogram in Ménière's.

A further question arose on the reference of the Weber test according to the pitch: he thought this similar to the positive or negative Rinne according to pitch, which was obtained in many cases of otosclerosis.

On the question of hyperacusis, he felt that that would fit in very well with the President's view of a toxicemic condition. If it were a toxic neuritis one would expect an early stage of hyperacusis, just as in many other examples of peripheral neuritis one had an early stage of increased localized sensitivity; tinnitus would fit in very well with that as a form of neuralgia.

Mr. Terence Cawthorne said that the President had made an important reference to paracusis or diplacusis. One of the most characteristic features of perceptive deafness accompanying or preceding Ménière's disease was dislike of loud sounds and particularly of loud high-pitched sounds. It was a very common thing for a patient with Ménière's disease to volunteer the information that he could not bear to listen to music on the wireless, shrill voices or to children. Some sufferers could not have a meal in a restaurant because they found the clatter of knives and forks on the plates unbearable.

Sometimes one was faced with a patient who had very little hearing left and a decision had to be made whether the labyrinth should be destroyed or the vestibular portion of the nerve divided by an intracranial operation in an attempt to save the hearing on the affected side. Given a normal, or almost normal, ear on the sound side, he thought that no patient with Ménière's disease would ever thank the surgeon for leaving him with distorted hearing. On the contrary, he had often found that after a patient had been relieved of his distorted hearing he was once again able to enjoy the everyday noises of civilization.

He entirely agreed with the President that a very characteristic feature of Ménière's disease was the variability of the hearing. He had heard it said on more than one occasion that the perceptive deafness did not get better but always worse; but there was no doubt that in the type of perceptive deafness under discussion variability was the rule.

One important point was the negative Rinne. It was a physical sign of severe unilateral perceptive deafness that a patient could hear the tuning fork better by bone conduction than air conduction on the affected side. He had years ago been caught by this in a rather hurried examination, mistaking a perceptive for a conductive deafness, because of an apparently negative Rinne. In every case of unilateral perceptive deafness of severe intensity there would be a false negative Rinne, as could be shown quite well by masking. It was, he felt, that false negative Rinne which had led to the widespread belief that one of the commonest causes of Ménière's disease was Eustachian obstruction. His own experience was that Eustachian obstruction was very rarely seen in association with Ménière's disease.

Mr. Michael Vlasto said that a personal experience might be of interest. About six months ago he developed a sudden slight nerve deafness on the right side. He had been afraid that it might be a precursory symptom of Ménière's disease. But he had had neither tinnitus nor vertigo. He consulted three colleagues who kindly thoroughly investigated his case which included the puncture lavage of one slightly infected antrum. They had advised his giving up smoking. The most distressing feature of his affection in its earliest stage was a “Punch and Judy” effect of high pitched voices. This feature had now disappeared and his condition was otherwise stationary in spite of a resumption of smoking. Would the President kindly give his views on the possible ill-effect of smoking on his condition, and also as to the prognosis.

Mr. F. McGuckin had long been interested in Eustachian obstruction and, though there might be other causes, he had noted the following: trauma, adenoids, œdema of the torus tubarius, and neoplasm. In no case of proved Eustachian obstruction had there been any complaint of vertigo.

Mr. H. V. Forster said that he would ask Mr. Wright if he was in agreement with the theory held by Mygind and Dederding that certain cases of intermittent inner-ear deafness, associated at times with vestibular vertigo were caused by disturbance of the water metabolism of the body. Had he confidence in their method of treatment by reducing water and salt intake in the diet?

He, Mr. Forster, had personal reasons for believing that such passing attacks of inner-ear depression were associated with temporary loss of hearing for C32, with distortion of the tone of C₅₁₂ and perhaps later with some permanent loss in the higher “frequencies”.

Dr. Hugo Frey said that he found it a very interesting fact that the President was able to show that as a rule the cochlear apparatus showed signs, much earlier than the vestibular apparatus, of approaching Ménière's disease. He thought the explanation of this was that, on the whole, the cochlear apparatus in the human ear must be regarded as belonging to a later period of development. It was known that the lower classes of animals had no cochlear apparatus nor any acoustic perception; also it was found that in congenital deaf-mutes where there was malformation of the inner ear there were, with few exceptions, defects in the cochlear part of the inner ear, but not in the vestibular part. They gave when tested the vestibular reaction but very little or no cochlear reaction, which showed, *inter alia*, that the special factors which might be blamed for the deformity

of the ear in these cases must act during the period when the vestibular apparatus had already been formed but the cochlear apparatus had not yet been developed.

There was one annotation to be made. Everybody, he was sure, had seen cases of typical Ménière's disease or attacks in which no disturbance of hearing occurred. These cases were rare, but they did exist. In such cases it was necessary to conclude that this was a different sort of Ménière's as compared with ordinary cases.

He thought also that it would be highly desirable if somebody interested would survey again the whole of the tuning-fork tests in view of the present possibilities of improved acoustic methods. The tuning-fork tests were still based on statements and findings which were made more than sixty years ago. The original Weber test was not really meant as a test. What Weber did was to note the fact that if the tuning-fork was put in the middle line of the skull and one ear closed with the finger, the sound of the note was perceived in the closed ear. The Weber test as well as the Rinne test well deserved to be examined more closely, because no one, so far as he knew, was aware of what difference in hearing power between the two ears must exist in order to produce a Weber result. On the other hand, it might possibly be that the Weber test was so fine a test that it showed lateralization in the cases where no other means of testing the hearing showed anything to be wrong.

As regards Mr. Cawthorne's comments on the Rinne test, he had always been of opinion that in cases with more than a certain amount of hearing defect the Rinne test became unreliable. Not everything was quite clear as yet about the Rinne test. When they began to undertake surgical destruction of the whole labyrinth they found that afterwards, when everything was healed, in many of these cases, with one destroyed labyrinth, the tuning-fork was referred to the operated side. There must be something in the acoustic conditions of the bony skull which furnished the reason for this, but as yet it was not understood. The President's explanations, valuable in themselves, might induce further study.

Mr. Ian Robin asked how long one waited in a case of unilateral deafness and tinnitus, before vertigo arose, while making a diagnosis of Ménière's disease. Was it necessary to have tinnitus to diagnose Ménière's? If there were deafness and vertigo without tinnitus could that be put down as Ménière's?

The President, in reply, said that he had intended to present quite a simple little picture of one facet in this very involved and complicated disease. They had described cases of Eustachian obstruction with perceptive deafness, treated them, and all the deafness disappeared. How common was that? So many individuals had said that it occurred that he must accept it, but how often did it occur? He thought it was very rare.

He could not see any reason why there should not be hæmorrhages in the cochlea and thrombosis in a vessel; it would seem inevitable. Twenty years ago he used to write to the doctor and say that that was what he expected had happened, but he thought personally that the general picture showed that the vascular element was not the usual one.

He, the President, thought that Mr. Vlasto had experienced the same condition in a minor degree. When these conditions started in a minor degree they usually remained so, and in Mr. Vlasto's position, if his pipe were a great joy to him, he would continue with it. On the other hand, if there were any dead teeth he should have them out. The "Punch and Judy" sound was quite typical. That type of distortion was the sort of thing that patients told one about, and it was probably diagnostic, and was found only in this type of cochlear deafness.

The President, continuing, said that the prognosis was particularly good, especially in a mild condition which remained mild.

On the question of injury as the first step in a progressive change in the labyrinth he could not tell how often a progressive lesion was found following an injury. He saw a lot of cases with progressive changes in the labyrinth, and in a few of these there was a history of injury.

In reply to Mr. Forster, he had always found that general picture of interstitial oedema and so on rather vague. He remembered that at Copenhagen several patients were shown with classical Ménière's disease and various things were picked out and they were asked whether they were not all abnormal. Frankly he did not think so. He thought the evidence that reducing people's fluid intake did diminish the severity of their symptoms was fairly established. A large number of intelligent observers had produced evidence to that effect. But it had its risks. He saw a man in a nursing home who was getting renal colic because of oxaluria and he had oxaluria because he had Ménière's disease and had stopped drinking; he had been drinking only small quantities for some years. He advised him to drink and to have his teeth out.

On the question of the motor-car and the vertiginous driver, it was hard to say how big was the risk. Probably it varied in each case. His experience had been that there was practically always enough warning to enable the driver to run on to the side of the road and put on the brakes. But there was a very serious legal position over certification, and if the question was put as to whether attacks of giddiness were experienced, it was necessary to say that they must not drive a car. Apart from the legal question, he did not believe that the risk of accident resulting from an attack of vertigo was a very serious one.

He had been asked how long one should wait in a case of defective hearing before deciding that the defect was due to the condition they had been calling Ménière's disease. He would not wait at all. His object had been to present a plea that this could be recognized at the beginning, that one did not have to wait for vertigo, which might never happen, but that the auditory picture was the same one in this stage as it was in the established condition.

[December 7, 1945]

Vestibular Injuries

By TERENCE CAWTHORNE, F.R.C.S.

INTRODUCTION

THIS paper is based upon a study of the effects of deliberately destroying the end-organ of the vestibular nerve in the labyrinth for the relief of Ménière's disease in 120 cases and upon the detailed otological examination of a series of 58 closed head injuries whose convalescence was protracted mainly on account of disturbed balance.

In both groups, once the immediate effects of the injury had been overcome and the patients were ambulant, vertigo, easily provoked by sudden head movements, was the predominating symptom; whilst the most constant, and in many the sole physical sign, was an abnormal response to caloric stimulation of the labyrinth. Moreover, it was found that all these cases required the same management to aid in restoring balance and thus encourage their return to normal.

The striking similarity between the two groups, both as regards clinical features and management, led us to consider that the injury was probably in the same place in some cases, though of course it varied both in mode of production and in extent.

It is certain that in the case of labyrinthectomy it is the end-organ of the vestibular apparatus which is damaged, but as yet there is no pathological evidence available to show end-organ damage in cases of vertigo following head injury. Nevertheless the close clinical relationship between the two groups of cases leads one to believe that in both it may be the end-organ in the labyrinth that is the seat of the damage and this belief is further strengthened by the similarity of the physical signs.

The association of vestibular damage with head injuries was noted by S. H. Mygind (1918) who found that 24% of the cases he had examined had genuine vestibular symptoms. Brunner (1928 and 1940) stressed the importance of noting any nystagmus, particularly on altering the position of the head. Barre and Greiner (1932) found vertigo in 54 out of 100 cases of head injury though otological tests did not reveal any correspondence between cochlear and vestibular changes. Linthicum and Rand (1931) urged that post-concussional vertigo should not be dismissed without detailed neuro-otological tests, and Voss (1934) suggested that the term "labyrinthine concussion" might be used for these cases. Glaser (1937) found vestibular abnormalities in 76% of 66 cases, most of which he attributed to central changes. Barmoe and Marks (1941) stressed the value of a full otological examination in all cases of head injury followed by vertigo and mentioned the importance in the caloric test of using both the hot and cold stimulus to bring out any latent tendency to nystagmus.

In the general descriptions of concussion the frequency of vertigo as a sequel of head injury was particularly noted by Osnato and Giliberti (1927) and by Symonds (1937 and 1943) and Russell (1932), all of whom appreciated the possibility of vestibular disturbance in such cases.

MODE OF INJURY

(a) *Labyrinthectomy* (Cawthorne, 1943).—The site and mode of injury in the cases of labyrinthectomy that we have studied are quite clear. After opening into the perilymph space the membranous external canal is seized and removed. This has always resulted in a total loss of vestibular as well as cochlear function. We have found that the same result follows merely opening the endolymph space by tearing the membranous canal across or by coagulating the membranous canal with diathermy.

(b) *Labyrinthotomy*.—Another form of deliberate operative injury to the labyrinth that I think deserves mention is the opening of the perilymph space for the relief of deafness. Here the injury to the end-organ should be slight because an essential precaution of the operation is to avoid damage to the membranous labyrinth. Nevertheless, even when one can be reasonably certain that the membranous labyrinth has not been touched the disturbance produced is instantaneous and considerable and must be due to altered physical conditions rather than to direct injury or inflammatory reaction. This aspect of labyrinthotomy requires careful consideration because it has been my experience that in such cases vertigo forms a prominent and sometimes protracted feature of the post-operative course and prospective candidates for this operation should be warned

beforehand that they may be troubled by vertigo afterwards. They are, of course, helped by the same management as the other cases under consideration.

(c) *Post-concussion*.—Certain experimental work has been done to show that head injuries may be accompanied by changes both in the vestibular end-organ and its connexions in the central nervous system. Brunner (1928, 1940) found that blows on the fixed head caused changes in the peri- and endo-lymphatic spaces and also certain changes, mainly vascular, in the brain-stem as well as in other parts of the central nervous system. More recent work by Denny-Brown and Russell (1941) has revealed that the clinical picture of concussion could be easily produced experimentally by blows from a hammer with a striking speed of up to 40 feet per second upon the occipito-parietal region of animals whose heads were free to move with the impact of the blow. They termed this "Acceleration Concussion". Similar injuries to a fixed head they termed "Compression Concussion". A much smaller striking force was required to produce acceleration concussion than compression concussion and was attributed to a direct physical injury to the neurons which was reversible. It was obtained in the decerebrate animal both with and without section of the 8th nerves.

Nearly all the concussion cases with prolonged vertigo that we have observed were the result of acceleration concussion and I think that there is a very good reason why this is so.

As both the cochlear and vestibular end-organs rely for their essential stimulus upon displacement or deformation by a movement of endolymph, it is reasonable to suppose that if one end-organ suffers actual damage from over-stimulation by excessive endolymph movement, then over-stimulation may in a like manner cause damage to the other end-organ.

In the case of the cochlea, it is known that exposure to loud sounds (e.g. gunfire, boiler-making) may result in a disturbance of the cochlear fluids that is sufficient to cause permanent damage to the organ of Corti.

In the vestibular part of the labyrinth the end-organs (maculæ of the utricle and cupulæ of the canals) are so designed as to be exposed to pressure or traction by displacement of the endolymph in response to acceleration and deceleration movements of the head. As the maculæ and cupulæ are stimulated by the slightest and gentlest movements of the head, it is reasonable to assume that they would be exposed to a heavy strain when stimulated by the sudden and violent jerking of the head that is part of acceleration concussion. It might, therefore, be expected that the vestibular end-organ in the labyrinth would be particularly vulnerable to injury in concussion. The facts that vertigo is the cardinal symptom of a damaged labyrinth and that a frequent sequel of concussion is vertigo support this hypothesis and I hope that it may be possible at a later date to produce more concrete evidence to show that the vestibular end-organ is not infrequently injured in acceleration concussion.

CLINICAL FEATURES

The symptoms and signs that follow immediately upon an injury to the labyrinth are widespread and are often so terrifying in their intensity that observers unused to the ways of the labyrinth may find it difficult to believe that such a profound disturbance can be caused by injury to such a modest organ.

The overwhelming vertigo, the awful sickness and the turbulent eye movements—all enhanced by the slightest movement of the head—combine to form a picture of helpless misery that has few parallels in the whole field of injury and disease.

This lurid picture is, of course, seen when a previously active labyrinth is completely and suddenly overwhelmed and might conveniently be known as the syndrome of acute vestibular failure. The intensity of the symptoms will, however, vary from case to case, depending upon the nature and extent of the injury and they may sometimes be masked by the effects of injuries elsewhere. Fortunately the body is soon able to adjust itself to altered conditions even if normal balance between the two labyrinths is not quickly restored, and within a few days of injury the acute phase dies down, leaving a residue of effects which deserve our very careful attention. This residue is seen after operations on the labyrinth and in the so-called post-concussion syndrome where vertigo in one form or another plays a prominent part. The vertigo, giddiness or dizziness consists of a sensation of apparent movement, either of the subject in relationship to his surroundings or of the surroundings in relationship to the subject. The direction and extent of the apparent movement are immaterial. The essential feature is a sensation of movement that does not, in fact, take place. It is typically provoked by sudden alteration of

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posture or by sudden turning movements of the head. In most cases it is momentary, but in the postural giddiness induced when the head moves forwards or backwards, the sensation may remain for some time, though if the patient can be persuaded to maintain the offending position, the symptom gradually dies down, usually within a minute. In such cases there may be an accompanying nystagmus lasting for about the same time as the vertigo.

In the momentary vertigo following sudden head turning it is not often possible to observe any involuntary eye movements, though sometimes a fleeting flicker may be present. This is the common picture following labyrinth operations and many concussion head injuries. In another group of head injury cases the complaint may be one of continuous slight movement of the ground as though on a slightly rolling ship.

Frequently after labyrinthectomy and sometimes in the post-concussion cases there is a complaint of inability to focus the gaze upon an object for any length of time and of a dislike of looking at quickly moving objects. This is often sufficient to demand an ophthalmic examination which, however, rarely reveals any significant change.

Instability in the dark and on moving up and down stairs or on an inclined plane is usual and, as you will hear later, is catered for in the treatment. A tendency to tire quickly on physical exertion is almost the rule, particularly after labyrinthectomy, and it has been found advisable to warn patients that their return to normal life may have to be gradual and will depend largely upon their ability to overcome this fatigue.

If all these symptoms are not given careful attention and particularly if any adequate explanation is not forthcoming for them, a sense of insecurity may be engendered which will encourage the patient, particularly if he is of an unstable temperament, to drift into a state of chronic invalidism sometimes amounting almost to helplessness.

Headache, which is such a common sequel of concussion, is usually not seen after operation on the labyrinth and cannot, I think, be considered as part of a vestibular disorder, though it may be a most distressing and intractable feature of the post-concussion state. In long-standing cases there is sometimes an excessive and even bizarre disturbance of balance that is clearly out of proportion to the physical signs.

Out of the 58 cases of head injury which were submitted to a full otological examination 56 showed deviations from the normal in their response to caloric stimulation of the labyrinth according to the technique first described before this Section by Hallpike in 1942.

TABLE I

Total cases	58
Abnormal caloric response	56
Directional preponderance	39
Canal paresis	17
Normal caloric response	2

and more fully elaborated by Fitzgerald and Hallpike (1942) and Cawthorne, Fitzgerald and Hallpike (1942) (Table I). Of the remaining two cases, in one the vertigo had disappeared some days before the caloric test and in the other a transient dizziness on bending down had been experienced ever since a head injury two years previously. Of the 56 cases who showed an abnormal vestibular response only 24 had damage to the cochlea (Table II).

TABLE II

Normal hearing	34
Directional preponderance	23
Canal paresis	9
Normal caloric	2
Abnormal hearing	24
Directional preponderance	16
Canal paresis	8

These findings strengthen my belief that in persistent vertigo following concussion the vestibular end-organ is a likely seat of the damage. I would like to emphasize that signs of such damage can only be demonstrated by a careful and detailed otological examination.

TREATMENT

The impression that we have gained from our observation of these cases during the past eight years is that the disturbance of balance caused by an injury to the vestibular apparatus has a profound effect on the well-being of the patient. This is not surprising when we recall that the sense of balance is one of the most primitive faculties with which we are equipped, appearing in the biological scale before the senses of sight and hearing

and possibly before the senses of taste and smell, though of course it has not as yet been elevated to the dignity of a "sense".

To the more impressionable patients a labyrinthine disturbance may make them feel that the end of the world has arrived and I am told by sufferers from sea-sickness that in the acutest phase of their distress, they wish that it had.

Hence it is not surprising that the clinical picture which we have been considering is not infrequently complicated by psychological disturbances which may be sufficient to divert attention away from the underlying cause.

We have found that once the true nature of the disturbance has been established an explanation of the state of affairs, combined with graduated exercises especially designed to encourage head and eye movements, form the most satisfactory basis for hastening recovery (Cawthorne, 1945).

Since the head exercises, which Dr. Cooksey will describe, were instituted by him and carried out by Miss Swan and Miss Hudson at Horton Emergency Hospital, the rate of recovery after operations on the labyrinth has been greatly hastened and we now expect that such cases can resume their normal occupation from within a month of operation, though of course it may sometimes be advisable to recommend a change of occupation. The post-concussion cases, for whom these exercises are particularly useful can, if they are tackled reasonably soon after injury, usually be prevented from drifting into chronic invalidism. The poorest responses to exercises and rehabilitation were always seen in those cases which had been allowed to drift for months with but little planned treatment.

The management of these cases has been made easy and pleasant for me and for my patients because of the way in which it has been possible for Dr. Cooksey and his assistants, the clinicians and ward sisters, all to work together and to share the problems raised by these cases.

I shall always be grateful to Dr. Cooksey and his assistants for their help and to my colleagues at King's College Hospital, the National Hospital, Queen Square, Horton Emergency Hospital and Hurstwood Park Emergency Hospital and to friends elsewhere for referring their cases to us. We have been able to help some, we have failed with others, but I know that we have learnt a lot from all of them.

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Rehabilitation in Vestibular Injuries

By F. S. COOKSEY, O.B.E., M.D.

IN 1941 Mr. Cawthorne put to me the principles governing the restoration of fitness after injury to the vestibule and sought my help to develop a system of rehabilitation for these cases. It happened that about the same time I had arranged with the Staff of the Head Injury Centre at Hurstwood Park Hospital to undertake the rehabilitation of late cases of the post-concussion syndrome in my Department at Horton Emergency Hospital. Thus the system of rehabilitation which I am about to describe was developed for the post-concussion syndrome as a whole as well as for the particular problem of vestibular injury.

The symptom complex for which I had to provide consists of headache, vertigo including the so-called "black-outs", impaired mental concentration and deafness in a proportion of cases. Of these symptoms the vertigo may be the most disturbing; but, fortunately is usually amenable to treatment along the lines I shall describe.

Unfortunately the headaches are often persistent and difficult to alleviate. They tend to be severe and have the double disadvantage that they are easily induced by physical or mental effort and are common on first waking. Thus patients are apt to start the day disinclined to engage in any form of rehabilitation. Even if they avoid waking with a headache they find by experience that noise, bright light, talking to a group of people, reading and physical effort bring on a headache. In similar manner the vertigo can be controlled by slow and deliberate movement, but the quick movements of spontaneous activity readily precipitate an attack. Under such circumstances it is natural that, when left to their own initiative, patients seek solitude and inactivity. It might be expected that the symptoms would disappear with the lapse of time; but in many cases this is not so and it is a common experience to see patients with little or no improvement after a year or longer. We believe that failure to recognize the vestibular lesion together with failure to provide adequate measures to restore confidence and to compensate for the damaged vestibular function are the reason for the undue persistence of symptoms.

It has long been recognized in disease and injury of the locomotor system that spontaneous restoration of function does not always follow resolution of the original lesion. Moreover the convalescence of all cases is shortened by systematic measures to assist the recovery more especially when treatment is instituted at the earliest possible moment. We decided to apply the same principles to our patients with concussion injury and also to those cases in which the vestibule had been destroyed in the operative treatment of Ménière's syndrome. We employ graduated physical exercise, mental exercise and occupational therapy. We find that patients can overcome their disabilities by constant encouragement and practice; also, subject to certain limitations in head injuries, the earlier we commence rehabilitation the quicker and better the results.

I attach great importance to four points: First, the initial interview with the patient when we seek to gain confidence and co-operation by explaining the nature of the symptoms and purpose of treatment, with special emphasis on the need to make regular and gradually increasing efforts to do just those things which they find distressing. Secondly, domestic and occupational anxiety must be relieved at the outset by assuring the patients that they will be able to return to their normal work or, if this is unlikely, by explaining the opportunities for vocational training and the operation of the Disabled Persons Employment Act. In this connexion the services of an experienced almoner are essential. Thirdly, a single member of the rehabilitation team should be made responsible for the welfare of these patients and be present whenever they are seen by the surgeon. Fourthly, the programme of physical exercise, mental exercise and occupational therapy should be planned to occupy the whole day and at the same time allow adequate periods for rest between the various activities.

PHYSICAL EXERCISES

The exercises are designed to restore balance as far as possible and to train the eyes and muscle and joint sense to compensate for permanent vestibular dysfunction. Because so many patients are worse in the dark we pay special attention to muscle and joint sense by performing many exercises with the eyes closed. Patients start with individual exercises in bed. In the case of simple concussion exercises may start at seven days. Fractures of the base may start at three weeks and other fractures of the skull as soon as the condition of the patient warrants. In the operative treatment of Ménière's syndrome patients learn the exercises prior to the operation and commence treatment the day after the operation. The time to start exercises must be determined for each patient by the surgeon, but the general rule is the sooner the better.

As soon as patients are able to get up, even if only in a wheel chair, they do their exercises all together in the gymnasium. It is a great advantage to group patients for exercises. In the first place patients encourage each other and those at the beginning of treatment see the progress made by the more advanced cases. Various games can be introduced to vary the monotony of purely remedial exercises. It is economical of staff and all patients receive thorough treatment whereas, in a busy department, individual treatment is time-consuming and apt to be scamped. Moreover the slacker or true malingerer has little chance of escaping exposure by fellow patients with similar disabilities even though he may at first deceive his surgeon.

The table of exercises which is used at each session starts with slow and easy sitting exercises which all patients can manage. First a few loosening movements for the head and shoulders; then head movements with the eyes focusing on near and distant objects; followed by head and arm movements with the eyes closed and directing special attention to training the sense of position in space. Next the movements are speeded up, and slow and quick movements alternated. At this point the beginners drop out and the remainder

progress to similar exercises in standing. Finally only the comparatively fit patients remain for such exercises as walking up and down steps and ladders, first with the eyes open and then with the eyes shut; games with balls and bean bags, when the instructor tosses a ball, high or low, which the patient catches, holds above his head, turns smartly about and bends down to throw the ball back to the instructor between the legs. It is surprising what patients will attempt when spurred on by the instructor and fellow patients. We have seen no untoward effects and it is our experience that, within reasonable limits, the earlier patients are urged to attempt the more difficult exercises the quicker they regain confidence and balance.

In the final stages patients are transferred to the general physical training exercises in which they mix with patients convalescent from various types of disease and injury. In the case of patients who have to return to occupations involving climbing ladders we endeavour to test them out on a small assault course we have built in the hospital grounds. The exercises are under the direction of a physiotherapist who holds a University diploma in physical education.

MENTAL EXERCISES

Many post-concussion patients complain of lack of mental concentration and to assist recovery the education officer takes these patients for an hour each day. By means of play-reading, debates, "brains trusts" and organized study, patients are trained to concentrate on increasingly difficult subjects.

OCCUPATIONAL THERAPY

This combines physical and mental exercise for the purpose of creative work. The object in these patients is to train them to concentrate and to perform the quick and involuntary movements of normal activities. It is useful also to train patients to work under crowded and noisy conditions. Patients start with sitting work involving minimal concentration in the quiet light-handicraft workshop. As they improve they progress to work which involves more concentration and more moving about, including bending and stooping. Finally they progress to the carpentry shop where noise and hard physical work will either restore their confidence to return to industry or reveal the failure of the earlier treatment.

INDUSTRIAL RESETTLEMENT

Rehabilitation in vestibular injuries is not complete until the patients are returned to their normal work or satisfactorily resettled. Patients who are unable to return to their normal work and in whom the disability is likely to last at least six months are qualified to register as disabled persons. Inclusion on the register entitles these patients to vocational training and placing in suitable work. On the recommendation of the surgeon the almoner will arrange with the disablement resettlement officer at the patient's local office of the Ministry of Labour for registration, vocational training and placing in employment.

If it is possible to combine the few cases of vestibular injury with other head injuries and any medical cases of vertigo, grouping them together, it has the advantage of increasing the size of the group. The principle on which we are working is equally applicable to them all.

Mr. Cawthorne now takes his cases of Ménière's syndrome into hospital a week or two before operation, and while he carries out certain investigations, the patients attend exercises in the gymnasium along with the convalescent cases, so that they begin to learn the exercises and are encouraged by seeing the progressive recovery of these other patients. The orthopaedists have also found that to teach patients exercises before operation makes the job much easier afterwards. The time to start the exercises after operation must be determined by the surgeon in each case, but the general rule is the sooner the better.

[At the close of Dr. Cooksey's paper two members of his staff, Miss Swan and Miss Hudson, gave a demonstration of the exercises, one acting as instructor and the other as "patient".]

The President said that in the first place, Mr Cawthorne had pointed out that it was not very infrequent for a pathological lesion to be found in one portion of the labyrinth.

It was a point not sufficiently recognized that while the labyrinth was one organ, and as a rule did suffer disturbance as a whole, both in its auditory and vestibular portions, it was not infrequent, either as a result of disease or of injury, to get a pathological lesion confined to one part.

Mr. Cawthorne was, he thought, a little puzzled as to the explanation of why eye movement should produce a considerable degree of disturbance, as it did in patients with labyrinthine lesions. The eye picture was a very large part of the whole picture. Surely if it was considered that as a result of abnormal sensation from the labyrinth a central disturbance occurred, then all the other sensations as they arrived at the centre were liable to produce abnormal sensory reaction.

After all, the sensations did not arise in the end-organ: the abnormal sensations arose at a higher level. He thought that the answer was that the higher level became disturbed, and all these exercises they had been witnessing were really examples of re-training at the higher level. At least that seemed to him to be the sort of outlook that a simple-minded non-scientific man might take.

He had been interested in Mr. Cawthorne's remarks on acceleration and concussion. In the past one had imagined that concussion was the result of a blow upon this "box" within which there were certain important structures, but he gathered that in quite a proportion of cases of concussion the injury was produced by movement of the head and not by a blow upon the head. That was an important point. He thought it was very probable that his suggestion that a great part of the picture was produced by this movement on the vestibular apparatus was the correct one, but he rather gathered that Mr. Cawthorne was hoping that some experimental work might be done to furnish support for that hypothesis. He had not himself observed that the patients who had a labyrinthine destruction were more easily tired than others, but seeing that their whole locomotor system worked rather abnormally one might expect that there would have to be a rather greater nervous effort made to produce the same output.

He had been taking advantage of the experience gained by Dr. Cooksey's work in the rehabilitation of cases following labyrinthine destruction, and he had been most impressed; he had entirely altered the outlook on the post-operative phase. His own practice was to get these people out of bed on the third or fourth day and one had a picture within two or three weeks that formerly was not obtained for two or three months even if then. He was sure that mass psychology was a very valuable thing to introduce into rehabilitation.

Mr. E. D. Davis said that he could foresee the time when rehabilitation could cure vertigo and the labyrinth operations would be unnecessary. He had had some experience of injuries to the head during the war of 1914-18 and of a number of cases during the recent war. The large majority of fractures of the skull involved the middle fossa and the middle ear. The fracture took the line of the Eustachian tube and the roof of the tympanum and the mastoid antrum and the labyrinth was very rarely injured. It was difficult except in very severe injuries, mostly fatal, to see how the internal ear could be injured because it was encased in the hard petrous bone surrounded by the bony capsule of the cochlea and semicircular canals filled with perilymph and endolymph. He had the notes of 57 cases of injuries of the ear as the result of fracture of the skull and only 5 of these showed any signs of injury to the internal ear. The injury was limited to the cochlea and the labyrinth was normal except in one case. The majority of the patients with fractures of the petrous bones died. Hogarth Pringle (1939) recorded 366 cases of fracture of the skull of which 39 post-mortems showed fractures of the posterior fossa and all the patients who were suspected of having a posterior fossa fracture died. It is the fracture of the posterior fossa which involves the petrous bone. During the war of 1914-18 he was a neuro-surgeon at a casualty clearing station and he only saw about three cases with injuries to the posterior fossa. Most of these cases died on the field of battle.

Gordon Wilson who studied the effect of injuries on the ear (1914-18) stated that it was very rare to find a damaged vestibular apparatus; it was almost always the cochlea.

The injuries to the internal ear could be divided into three groups.

The first group consisted of cases of undoubted and permanent injury to the internal ear showing marked deafness, paralysis of cranial nerves, escape of cerebrospinal fluid, &c. If the hearing did not improve in eight weeks the loss of hearing was permanent. Some of these cases were tested for damage to the vestibular apparatus after recovery from the head injury. The caloric and other tests showed a normal vestibular apparatus in all except one or two.

The second group comprised the so-called cases of psychical deafness. The deafness was usually bilateral and accompanied by other mental and vasomotor disturbances. The hearing tests were often contradictory. When examining such cases it is important to ascertain the position of the patient with regard to the explosion causing the injury. Most injuries to the ear were unilateral and within about 20 feet for the average small bomb. If the patient is immersed in the sea or water the critical distance or danger zone is four times as great, 80 feet. The psychical cases are occasionally suspected of malingering.

The third group are those of temporary deafness, so-called concussion deafness. These patients perhaps sustained other severe injuries and by the time they had recovered from these the deafness had disappeared and the ears were normal. It is difficult to ascertain what anatomical injuries to the internal ear occur. The auditory nerve cannot be seen

like the optic disc but there is a comparison. It is doubtful whether concussion deafness actually exists.

The vertigo following head injuries and fractures of the skull is, in a number of cases, due to damage or contusion of the brain. These patients complained of varying degrees of instability, black-outs, tinnitus, confusion, &c., with normal ears and hearing. The fields of vision may be contracted. The symptoms are not like the rotatory vertigo with unilateral deafness and other signs seen in an aural vertigo. Rehabilitation is valuable for the head injury type of unsteadiness. His experience of the condition of the patient after operations on the labyrinth was similar to that of Mr. Cawthorne. These patients were distressed by intense vertigo and vomiting which took some time to disappear.

REFERENCE

PRINGLE, HOGARTH J. (1939) Some Fractures of the Skull, *Lancet* (ii), 1164.

Mr. F. W. Watkyn-Thomas said that in considering the effects of labyrinthine destruction they had to realize, as Mr. Cawthorne had said, that the labyrinth was part of one of the great protective mechanisms of the body. Its function was to maintain equilibrium; not only a constant relation to fields of gravitational force, but also a constant field of vision. All these things were keyed up on the labyrinth. This meant not only the compensatory movements but everything that went with them, such as the reciprocal innervation and the co-ordinated vasomotor reflexes. A disturbance of the labyrinth meant a complete upset of a mechanism which had been running smoothly for generations, and thus one got the extraordinary general response.

As to the description of labyrinthine vertigo he always recalled the Club of which Mr. Jorrocks was a member in which no member was considered to be drunk so long as he could lie still without holding on to something. It was this which made the recovery so difficult. A disturbance of the labyrinth owing to injury seemed to be a crushing disaster at the time. Curiously, the people whose labyrinths were destroyed for suppuration did not seem to suffer so much after it as those whose labyrinths were destroyed for the cure of Ménière's disease.

On the question of concussion in mastoid operations, he thought that the answer was that they were dealing with an incompressible part of the skull, with a part specially made not to give under a blow but to stand up to a blow. This was suggested by the carefully built-up petrous with its neat balance of hard and elastic bone. He had once or twice noticed some vertigo, after operating on a mastoid with very hard bone, and gougues were not up to the standard required. In one case this lasted long enough to make him fear that he had damaged the external canal, but events proved that all was well.

There was another point about concussion. It was fairly well shown that the crista was anchored at both ends, to the roof as well as to the ampulla. There was one case mentioned by George Jenkins in which a woman was throwing a child up and catching it, and suddenly she went down on to the floor; whenever she put her head into that same position afterwards she got such intense vertigo that Jenkins was compelled to destroy the labyrinth. He had attributed it to dislocation of an otolith membrane.

The question of rehabilitation was most important. Miss Wadge, his chief assistant, pointed out to him some time ago that the sooner one got a patient sitting up after a labyrinth operation the more quickly he recovered. The consequence of that was that they had cut down the time in bed to the very minimum. But it was a new and excellent idea to start these exercises before the operation was done.

Mr. E. D. D. Davis said that in concussion deafness the membrana tectoria was seen to present almost a vertical instead of a horizontal position in the microscope sections. Gordon Wilson had observed this in one case, and he thought it had been found in others.

Mr. H. V. Forster said that in his clear exposition of a difficult subject, Mr. Cawthorne had stressed the degree of suffering experienced by the patient in disorders of the vestibular nervous system.

At a discussion before this Section in 1937 McNally, *Proc. R. Soc. Med.*, 30, 905, had explained that in abnormal labyrinth stimulation the autonomic nervous system was set an almost impossible task of readjustment and how in the resulting confusion nausea was produced.

The labyrinth as an organ of special sense did not rank as high as that "distance receptor" the eye, over whose impressions throughout the ages of man's development the vast area of the cerebral neopallium had grown. But Sherrington nevertheless had described the labyrinth as "the chief proprioceptor of the leading segment of the body which is the head" and had given us a concise understanding of its physiology when he wrote: "The labyrinth keeps the world right side up for the organism by keeping the organism right side up to its external world." Sherrington, C. S., "The Integrative Action of the Nervous System" (1909), p. 336, London.

We could imagine that the congenital deaf-mute in a complete "black-out" would have little to guide him beyond the segmental proprioceptors of the trunk and limbs, but to fall then into deep water these too would fail him with an overwhelming sense of "disorientation". He, Mr. Forster, had been taught many years ago that such an event fulfilling these painful conditions had been recorded.

Mr. I. Simson Hall referred to the method of production of these labyrinthine symptoms. Mr. Cawthorne had stated his belief that they were due to the influence on the nerve

endings. One of the mechanisms was by tension or change in the fluid balance within the labyrinth acting upon the nerve endings. It was a point that deserved attention. Whether one injected alcohol into a labyrinth, ablated the labyrinth by operation, or merely made the smallest possible opening into the labyrinth to let out a little fluid, the symptoms were the same. A labyrinthine crisis of vomiting, giddiness and nystagmus was produced. His experience in making a small disturbance in the fluid of the labyrinth in the fenestration operation tended to show that the influence was through the fluid on the nerve endings.

Mr. C. S. Hallpike said that everybody who had studied this subject would know its difficulties, and he thought it would be generally recognized that Mr. Cawthorne's paper represented a very considerable advance. In particular the methods employed would commend themselves as the right ones to all interested in the scientific side of the subject. It was well known that oto-neurological views in the past had been based very largely upon obscure symptomatology, and not, as they should have been, upon physical signs. Mr. Cawthorne had now made it clear, probably for the first time, that it was possible in many of these cases to elicit meaningful physical signs from the affected vestibular system. From this point he hoped very much that further progress would be rapid.

Sir Milsom Rees said that he had been particularly interested in the 8th nerve, because he was almost sure that it was through this nerve that sense of location and direction was possible, and we were enabled to find our way about, with the aid of some form of magnetism. If this theory was correct for human beings it was likely to be so for birds and all other animals, including eels. Some years ago he read a paper to the Royal Society of Medicine on the role of the labyrinth, but the puzzle to him had been and still was, what part of the auditory apparatus actually gave the sense of location. It was old knowledge that birds and animals had an uncanny way of finding their direction and whereabouts, but how they found it had never been explained. He trusted therefore that some of those interested in the anatomy and physiology of the ear would test his own views on the subject and say whether he was right or wrong.

Mr. Terence Cawthorne said that Dr. Cooksey had stated that some of these cases deceived the surgeon. This was true and in doubtful cases it was often possible to pick out the patients who were "putting it on", by watching the head exercises class at work. It was most instructive to see the way in which the genuine cases behaved and on the other hand the way in which those who were "putting it on" staged their symptoms. Some of these latter would put on terrific turns, rather like a comedian on the music hall stage who pretends to be drunk and seems about to fall into the orchestra.

The President had spoken about the pathological lesion being in one part of the labyrinth. He was inclining more and more to the same view.

He was in agreement with Mr. Davis on the frequency with which fractures of the skull involved the middle ear. He had had the opportunity of seeing several such cases, giving rise to ear discharge and granulations, and in some of these cases the cochlea at any rate had been intact.

Mr. Watkyn-Thomas had mentioned the fact that in cases with suppurative labyrinthitis the vertigo was not so intense as after an operation for Ménière's disease. The reason for this was quite clear. The amount of post-operative disturbance was in proportion to the amount of immediate pre-operative function. In the case of the suppurative labyrinthitis it was possible that the function might have slowly disappeared, whereas in the case of Ménière's disease, particularly if there had been an active labyrinth, it was likely to have been suddenly cut off.

Mr. Forster had mentioned about throwing born-deaf children into baths. There was no reason why such children should not learn to swim because nearly all children born deaf gave an active response to vestibular stimulation.

Mr. Simson Hall had mentioned the altered fluid conditions, and he was sure that they might be expected to play an important part in vestibular disorders.

Dr. F. Cooksey, also in reply, said that he entirely agreed that mass psychology was the key to a large part of this problem. He himself had to be an enthusiast and insist that these patients be spurred on. Danger would only arise if the patients were not carefully selected in the first place by those, like Mr. Cawthorne and the members of the Section, who would guide them as to the essential scientific basis of the disability and principles of treatment.

Some Temporal Bones which had been Subjected to Mastoid Operations.—E. D. D. DAVIS, F.R.C.S.

Mr. E. D. D. Davis exhibited some interesting specimens which he had accumulated over a considerable period of time illustrating some of the naked-eye points in the anatomy and pathology of the middle ear and of operations on the mastoid and labyrinth. The fixing and embedding of the temporal bone in plaster of Paris made macroscopical dissection easier. Mr. Davis said that these specimens were very useful for post-graduate teaching.

Section of Laryngology

President—G. EWART MARTIN, F.R.C.S.ED.

[December 7, 1945]

DISCUSSION ON PENICILLIN IN RHINOLOGY

I. Simson Hall (*Abridged*): Some months ago when supplies of penicillin began to reach the teaching centres in greater quantities a series of experiments was undertaken, designed to explore some of the possibilities of penicillin treatment and to explain some of the good effects which we had already observed in our clinical work. Some types of infection were selected which seemed to be amongst the more urgent problems. These were the common cold, streptococcal infections of the pharynx, Vincent's angina, and sinusitis. The investigation was carried out in Edinburgh Royal Infirmary with Dr. J. F. O. Mitchell as part of the penicillin investigations under Professor J. R. Learmonth. I shall confine myself to cases of acute frontal sinusitis with complications.

These cases all appeared within a few weeks of each other and we were able to form impressions rapidly. Each case had osteomyelitis characterized by a doughy oedema spreading upwards through the hair line, two had subperiosteal abscess, one had meningeal irritation, and one established meningitis and frontal lobe abscess. The organism in three cases was the staphylococcus, in one non-hæmolytic streptococcus, and in one hæmolytic streptococcus. Treatment in each case followed the same lines. The only operative treatment carried out in my department was the insertion, through a one half-inch incision and a trephine hole, of a fine rubber tube into the frontal sinus. The tube was stitched to the skin and the skin closed round the tube. Through the tubes the sinuses were irrigated with saline and a known dose of penicillin was injected at frequent intervals. In one case a double intranasal antrostomy was also carried out. Continuous parenteral administration was also used. The result of this treatment was that all cases were healed and dry and without nasal discharge in less than three weeks: an average of seventeen days.

The case which developed frontal lobe abscess presented the full range of common complications and deserves comment. Our ophthalmological colleagues were of the opinion that the slight papilloedema present at first was due to the high intracranial pressure induced by the meningitis. The excellent progress of the patient seemed to support this opinion, but a return of lethargy and increased papilloedema proved that further treatment was necessary and the patient was transferred to the Neurological Unit under Mr. Norman Dott. Using the customary coronal incision the larger portion of the frontal bone was removed for decompression, and in doing so, the frontal sinuses

endings. One of the mechanisms was by tension or change in the fluid balance within the labyrinth acting upon the nerve endings. It was a point that deserved attention. Whether one injected alcohol into a labyrinth, ablated the labyrinth by operation, or merely made the smallest possible opening into the labyrinth to let out a little fluid, the symptoms were the same. A labyrinthine crisis of vomiting, giddiness and nystagmus was produced. His experience in making a small disturbance in the fluid of the labyrinth in the fenestration operation tended to show that the influence was through the fluid on the nerve endings.

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clear on the third day and was seen well three months later. In the fifth the organism was *Staphylococcus aureus*. The antrum was clear on the fourth day but the case was not followed up.

A further 8 cases of chronic sinusitis were treated. The results on the whole were disappointing. 3 developed blocked ostia and of these, 2 had intranasal antrostomies performed with satisfactory result. The third refused operation. 3 cases were treated with apparent success, and 2 further cases of chronic sinusitis were treated with penicillin and later required operation.

A further 4 cases of catarrh were also treated with apparent success. The histories varied from two to five years, the chief complaint being of post-nasal mucus. In none of these was there any gross sinus pathology and the clinical findings were congested nasal mucosa in all and excessive post-nasal mucus in 3. All were subjectively improved and in each case I noted an improvement in the appearance of the nasal mucosa. The longest follow-up was three months. These cases were all treated in the spring and summer of this year so that it is premature to pass final judgment on them.

J. F. O. Mitchell (*Abridged*): This report is on the local use of penicillin in the nose and throat.

The clinical work included both experimental and therapeutic applications, and these were controlled by bacteriological studies.

All swabs were at once inoculated on blood-agar plates and incubated for at least twenty-four hours. In addition direct smears were made from swabs of Vincent's infection; and in the case of swabs from patients who had already received penicillin, penicillinase blood-agar plates were used. When there was any doubt as to susceptibility to penicillin, sensitivity tests by the ditch method were performed, using a standard *Staphylococcus aureus* as control.

Penicillin in the mouth and throat.—There, a lozenge was used, and the best was found by experiment to consist of plain 8% agar with about 750 units penicillin. Lozenges could be made to last at least two hours and were administered so as to maintain a constant salivary concentration.

The first stage was one of clinical experiment to determine the efficacy of the lozenge and the best system of administration. It was proved by a series of experiments that administration of four lozenges at two-hourly intervals is enough to produce a sterile faucial field which remains so for about six hours. Practical systems of dosage were administration at 9 p.m., 1 a.m., 5 a.m., 7 a.m., and 9 a.m., for overnight pre-operative preparation, and two-hourly by day and once at night (10 lozenges per twenty-four hours) for maintenance of sterility.

Therapeutic trials were begun with tonsillectomy cases.

The clinical series concerned a total of 76 treated and control cases of tonsillectomy. The treated cases were grouped in three series according to the duration of penicillin treatment which was respectively three days post-operative, twelve hours pre- and three days post-operative, sixteen hours pre- and eight days post-operative. Cases were seen on fourth day, ninth day, and after four to six weeks, and the faucial condition recorded. The results show some striking improvements.

Penicillin therapy greatly improves the local condition and lessens the discomfort especially in the immediate post-operative period, the longer pre- and post-operative therapy giving the best results. In the final result, however, any benefit is much less marked and there it appears that surgical technique plays the major role.

By section of the tonsils removed it was proved that, even after three days pre-operative medication penicillin does not seem to penetrate into and sterilize the depths of the tonsillar crypts and therefore will not cure a chronic tonsillitis.

Vincent's infection also rapidly resolves under penicillin therapy. Treatment was one lozenge two-hourly by day and once at night. No other therapy was considered necessary. The results were almost immediate relief of pain and faecal, complete freedom from symptoms and bacteriological cure within two days, clinical cure and cessation of treatment in an average of four and a half days. There still remains the necessity to clear up any local predisposing factors such as carious or erupting teeth, or dental pocketing.

were removed. The lining of the sinuses was slightly thickened, and was sterile. The abscess was tapped at a subsequent operation and the patient has made an excellent recovery. One more fact may be recorded and that is the result of an observation made at the tapping of the abscess. Prior to this a large injection of penicillin (250,000 units) was given and on the first tapping no penicillin was found, but within a matter of minutes after the tension had been relieved, penicillin was found in the abscess contents, thus confirming the observation that, in presence of high internal pressure, penicillin does not penetrate into intracranial abscess cavities till the pressure has been relieved.

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To summarize: it is suggested that penicillin is no substitute for surgery but that the day of radical surgery as a primary treatment for acute infections of the frontal bone is over; that conservative treatment with penicillin is the treatment of choice until the acute infection is mastered, and that operative measures should follow later if necessary.

R. H. Hunt Williams (Abridged): In order to perfuse the sinuses with penicillin by local as opposed to systemic application one of two methods may be adopted.

First displacement therapy as advocated by Proetz may be used. Secondly repeated puncture may be carried out and the fluid injected. We employ a technique whereby one or at most two punctures of an antrum only are needed and the administration of penicillin left to the nurse.

After preliminary cocaineization the antrum is punctured in the usual way beneath the inferior turbinal with a trocar and cannula. The cannula should be of a slightly wider bore than the standard one so that after removal of the trocar it will easily receive a No. 12 ureteric catheter. A No. 9 catheter, which can be used with a standard cannula, has a slight tendency to become blocked. When the catheter is felt to impinge on the posterior maxillary wall it is withdrawn slightly. The cannula is then removed leaving in situ the catheter which is cut to a suitable length and fixed with strapping to the upper lip and cheek. The catheter ends just in front of the ear. For the frontal sinus I have only attempted this on one occasion. The frontal sinus cannula available was of a too narrow bore but it was found possible to use a fairly wide bore Eustachian catheter to act as a guide to the ureteric catheter which was then successfully inserted into the frontal sinus.

I do not think that perfusion of the ethmoid labyrinth by this method is likely to meet with success as it forms no adequate reservoir for the retention of the fluid.

A preliminary exploration of the sinus with a Watson-Williams syringe is needed in order to obtain a bacteriological report. Where penicillin is used the presence of resistant organisms such as *B. coli*, *pyocyanus* or *proteus* is a contra-indication.

Dosage.—The dosage had to be empirical. For local application of penicillin to other regions such as the eye, skin or deep wounds a strength of 250 to 500 units per c.c. is adequate. In order to get comparative results we employed a standard dosage in the earlier cases. 1 c.c. doses were given hourly by day and three-hourly at night for forty-eight hours and then three-hourly for a further forty-eight hours, 250 units per c.c. Total dosage was 14,000 units. In addition after the first forty-eight hours, the sinuses were irrigated before the morning and evening dose with 50 c.c. of warm saline and the nature of the washout recorded. This irrigation is not an essential part of the procedure but gives some indication whether improvement is taking place and whether further treatment is likely to benefit.

Later investigations showed that an aqueous solution of 12% sodium iodide which has roughly the same consistency as a penicillin solution and is radio-opaque will remain in an antrum from sixteen to thirty-six hours. The later cases were therefore given 5 c.c. doses at eight-hourly intervals, the total dosage in four days being 15,000 units.

Five cases of acute or subacute sinusitis were treated; 4 were cases of maxillary sinusitis, 1 was a case of pansinusitis; of these 5, 3 were members of air crew. 2 were back flying within three weeks and 1 in a month.

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clear on the third day and was seen well three months later. In the fifth the organism was *Staphylococcus aureus*. The antrum was clear on the fourth day but the case was not followed up.

A further 8 cases of chronic sinusitis were treated. The results on the whole were disappointing. 3 developed blocked ostia and of these, 2 had intranasal antrostomies performed with satisfactory result. The third refused operation. 3 cases were treated with apparent success, and 2 further cases of chronic sinusitis were treated with penicillin and later required operation.

A further 4 cases of catarrh were also treated with apparent success. The histories varied from two to five years, the chief complaint being of post-nasal mucus. In none of these was there any gross sinus pathology and the clinical findings were congested nasal mucosa in all and excessive post-nasal mucus in 3. All were subjectively improved and in each case I noted an improvement in the appearance of the nasal mucosa. The longest follow-up was three months. These cases were all treated in the spring and summer of this year so that it is premature to pass final judgment on them.

J. F. O. Mitchell (*Abridged*): This report is on the local use of penicillin in the nose and throat.

The clinical work included both experimental and therapeutic applications, and these were controlled by bacteriological studies.

All swabs were at once inoculated on blood-agar plates and incubated for at least twenty-four hours. In addition direct smears were made from swabs of Vincent's infection; and in the case of swabs from patients who had already received penicillin, penicillinase blood-agar plates were used. When there was any doubt as to susceptibility to penicillin, sensitivity tests by the ditch method were performed, using a standard *Staphylococcus aureus* as control.

Penicillin in the mouth and throat.—There, a lozenge was used, and the best was found by experiment to consist of plain 8% agar with about 750 units penicillin. Lozenges could be made to last at least two hours and were administered so as to maintain a constant salivary concentration.

The first stage was one of clinical experiment to determine the efficacy of the lozenge and the best system of administration. It was proved by a series of experiments that administration of four lozenges at two-hourly intervals is enough to produce a sterile faucial field which remains so for about six hours. Practical systems of dosage were administration at 9 p.m., 1 a.m., 5 a.m., 7 a.m., and 9 a.m., for overnight pre-operative preparation, and two-hourly by day and once at night (10 lozenges per twenty-four hours) for maintenance of sterility.

Therapeutic trials were begun with tonsillectomy cases.

The clinical series concerned a total of 76 treated and control cases of tonsillectomy. The treated cases were grouped in three series according to the duration of penicillin treatment which was respectively three days post-operative, twelve hours pre- and three days post-operative, sixteen hours pre- and eight days post-operative. Cases were seen on fourth day, ninth day, and after four to six weeks, and the faucial condition recorded. The results show some striking improvements.

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was tried, and in a third, although the interval was kept at four-hourly, the course was started twenty-four hours before operation. The usual starting time with the other two series was immediately the patient came round from the anæsthetic. Whichever method was used, we tried to make the penicillin administration as continuous as possible, allowing the patient respite only between the hours of 10 p.m. and 6 a.m., when he was sleeping.

Clinical results.—We realize that the series is too small to draw any dogmatic conclusions. Two of the symptoms recorded, namely pain and difficulty in swallowing, are subjective in character, and even the state of the tonsillar bed may give rise to differences of opinion. In addition, both the clinical and bacteriological results may be modified by concomitant sinus infection, previous attacks of quinsy, the degree of chronic tonsillitis, the presence or absence of adhesions, the interval between operation and the last attack of acute tonsillitis, and also the skill of the operator.

There were no outstanding differences in these respects between the penicillin-treated group and the control group. Consequently we feel that the two series are comparable.

All the tonsils were removed by dissection and the guillotine was not used.

The outstanding difference between the two series was the state of the tonsillar bed. The exudate that formed in the tonsillar bed of those patients who were treated with the penicillin pastilles was not nearly so marked. As a result the slough was not so deep and the wound healed with far less scarring of the faucial pillars. Fewer patients in this series complained of the late pain which shoots up to the ears when the slough is separating, and they appeared to swallow with greater freedom. With regard to the temperature, although there was no real disparity between the numbers of penicillin-treated patients and the control group who showed some rise in temperature, yet the rise was seldom so high in the penicillin-treated group, nor did it occur so frequently. This advantage was more obvious when we adopted the method of starting penicillin treatment pre-operatively, and in this series (10 cases) no rise of temperature was recorded, even on the evening of operation.

Bacteriological results.—Whichever method of administration was used, there was no appreciable difference in the bacteriological results. The sensitivity of all the organisms was tested against the Standard Oxford staphylococcus. Though it was not possible to indicate all the shades of variation in sensitivity that were found, the following divisions were made: (a) Sensitivity equal to that of the Standard Oxford staphylococcus; (b) sensitivity less than that of the Standard Oxford staphylococcus; (c) penicillin-resistant.

By the fifth day of treatment with penicillin it was found that there were definite changes between the two series as far as the bacteriological results were concerned. Whereas the plates from the control series still showed a mixed growth of the usual type, those from the penicillin-treated series were slimy in appearance with an easier differentiation of the colonies. Some of these were composed of non-sensitive "coliform" and diphtheroid organisms only: a few showed a scanty growth of sensitive staphylococci or streptococci, but in many there was quite a profuse growth of staphylococci which were of a penicillin-resistant type. Generally these colonies were mixed with some of the Gram-negative organisms and the cultural appearance suggested that they belonged more to the "*albus*" type than to the "*aureus*." As far as the other organisms were concerned the *Micrococcus catarrhalis* was generally sensitive, whilst the diphtheroids seemed divided in their sensitivity, some being entirely resistant. In two patients some penicillin-resistant pneumococci were cultured after penicillin treatment, though these organisms had not been found in the pre-operative swabs.

A further point of interest is the post-operative increase in the "coliform" organisms among the penicillin-treated group. It is now recognized that penicillin seems to favour the growth of these organisms and a similar result was obtained when the local application of penicillin was tried for the treatment of chronic suppurative otitis media.

In four patients who were given a pre-operative course of penicillin, the bacteriological flora was reduced to a few Gram-negative bacilli. After the tonsils had been dissected out, cultures were taken from the centre of the tonsils and in each case we obtained a profuse growth of *Streptococcus hæmolyticus* and *Staphylococcus aureus*. Both of these organisms were of standard sensitivity. This suggests that the local application of penicillin by means of pastilles will not cure a chronic tonsillitis. This is not surprising as, though penicillin is a very diffusible substance, it cannot be expected to penetrate to the bottom of the tonsillar crypts.

Acute streptococcal tonsillitis, another common condition, usually responds to the systemic use of sulphonamides. Penicillin lozenges now hold prospect of effective local antibacterial action coupled with the advantage of elimination of the patient's infective droplet spray. In early or catarrhal tonsillitis where the infecting organisms are as yet superficial, local penicillin therapy alone produces clinical and bacteriological cure within two days. When infection has reached the tonsillar crypts, however (follicular tonsillitis), it is in part beyond the reach of locally applied penicillin and with constitutional disturbance systemic sulphonamide, bismuth or penicillin is indicated, but cure is accelerated by the use of local penicillin also, which will attack the infection from the surface and at the same time sterilize the droplet spray. In my series, two identical cases were cured, one in three and a half days using systemic sulphonamide and gargles, the other in forty-eight hours using systemic sulphonamides and also penicillin lozenges.

The use of penicillin lozenges alone in a severe follicular tonsillitis will not prevent its progressing to *peritonsillar abscess*, since local penicillin does not penetrate the crypts, and once pus has formed, the condition demands surgical intervention.

Streptococcal carriers present a difficult problem to which no effective answer has yet been found. Although cases can sometimes be cleared by local gargles and paints and sulphonamides, relapse is common. Local penicillin clears them only as long as they continue to use the lozenges. Perhaps the combination of sulphonamides and prolonged local penicillin will provide the answer.

Penicillin in the nose.—There it was applied as a powder diluted with glucose to which was added $\frac{1}{2}\%$ menthol. Each patient received 86 mg. pure penicillin diluted to 2 grammes. Here also clinical experiments were deemed necessary, and these, although inadequate for final conclusions, showed that both the normal commensals and susceptible pathogens are rapidly eliminated by the use of penicillin snuff.

Therapeutic trials concerned its use in the treatment of the common cold and comparison with a control snuff of menthol $\frac{1}{2}\%$ in glucose, and with a proprietary suspension of "mickraform" sulphathiazole in paredrine. Penicillin and control snuffs were administered from a special glass applicator from which the patient inhaled a dose of snuff every two hours.

Cases, 38 in number, were divided into two groups, early and late. From these results it would appear that local penicillin snuff administered two-hourly for four days will effectively prevent the secondary invasion of pyogenic organisms (in every case in the trials), and if they have already gained a foothold, will completely eliminate the purulent discharge and produce cure in the majority of cases (6 of 9 trials) and considerably reduce it in the others.

Adjuvants to penicillin snuff were used in some cases. When nasal obstruction was marked and prevented the initial use of the snuff, 2% ephedrine-saline nose-drops, or menthol inhalations were used until adequate airway was obtained. In another case usually progressing to sinus catarrh and toxæmia, the latter but not the local symptoms responding to treatment in bed with sulphadiazine, the combination of local penicillin and systemic sulphadiazine produced complete cure within thirty-six hours.

E. G. Collins, P. D. Eeman, and A. R. T. Lundie: *Local penicillin therapy in tonsillectomy (Abridged)*: In February 1945 we started an investigation at a military hospital in Great Britain with a view to assessing the value of this form of therapy, and we attempted to determine the best method and routine of administration. There were 31 patients in the series which had penicillin treatment and 29 patients in the control series. They were not given sulphonamides in any form.

Bacteriological examination.—All the patients' throats were swabbed and bacteriologically examined pre-operatively, and in the first 20 cases post-operative swabs were taken on the third, fifth, seventh and ninth days, but later we reduced the post-operative bacteriological examinations to two: swabs being taken on the third and fifth days only.

Penicillin pastilles.—The first 10 cases were treated with home-made pastilles. Pastilles (lozenges) of 500 unit strength with an agar base were used for the remainder of the investigation; they lasted on an average about two hours.

Method of administration.—The pastilles were placed in the buccal sulcus, and the patient was instructed not to suck or chew them. The course lasted five days, but certain variations were made in the intervals of administration. In one series we gave the pastilles at two-hourly intervals, in a second series the effect of a four-hourly interval

R. J. V. Pulvertaft said that nothing had been mentioned about the inhalation of penicillin mists, but the subject had been much discussed in America and had been followed up in this country by Dr. Mutch of Guy's. He had tried it himself using the Collison inhaler. In the first place, the distribution of the drug was odd and unexpected with anything inhaled. It was chiefly collected on the turbinates and in the posterior pharynx, and after that in the œsophagus and stomach. It did not go down, in the earlier stages, through the trachea into the lung. It was concentrated in a very effective way in the turbinates and nasopharynx, but not on the tonsils. When inspired in this way, if a swab of the tonsils were taken it would be found that for a long time no inhibition was obtained at all on test plates. The drug was absorbed in the blood in highly bacteriostatic concentrations. It was too early to say that any result had been obtained in the treatment of nasal infections, and the treatment had the disadvantage that the patient went round smelling strongly of "cat". Much depended on the size of the particles introduced. If a relatively large particle mist were introduced by the Milton Dynalysor it tasted abominably, but given with a Collison inhaler in particles of 3 to 5 μ , it was quite sweet. Several patients said that their noses flowed more vigorously after inhalation. A great deal had been claimed for it in America, and it would be interesting to learn whether anybody had followed it up.

A. S. H. Walford said that it seemed to him necessary to find some method of dealing with the subacute and chronic case before any real good could be said to be done. He had found repeated instillation of the antra by inserting a trocar and cannula, as designed by Mr. Asherson, then withdrawing the trocar; leaving the cannula in situ for four or five days, to be effective. The antra could be sucked dry, and 2 or 3 c.c. of penicillin solution put in every six hours. He felt that theoretically that was more likely to work than most other methods, and in fact it did seem to work better. When they said that penicillin would not replace surgery he could not help thinking that that was defensive on their part, at least to some extent. It would not replace deep surgery, but he believed that if they knew how to use it, a great deal of surgery in acute cases would be abolished.

T. B. Jobson described the case of a lady aged 45, who in 1933 had a discharging antrum, which was opened and curetted first through the nose and a year later by Caldwell-Luc. The antrum still continued to discharge, and gradually it adopted a habit of discharging green crusts, which were washed out every few days. After ten years she came under his care, still discharging the green crusts, feeling ill, and having chronic headaches. Penicillin was given systemically every three hours and locally injected into the antral cavity. The antrum was washed out with saline first, and then the penicillin was injected. After ten days of that treatment the antrum was apparently perfectly clear. The washouts showed no pus or mucus, there was no green slough, and she had continued up to date with neither discharge nor headache.

In another case, a child of 7, on whom double antrostomy was done, all sorts of washings were carried out, but no form of irrigation seemed to make any difference. The child was then given only topical treatment with penicillin. She showed no improvement whatever for two weeks, still having a great deal of dirty slough, and then suddenly she changed, and the wash-out became perfectly clear. She had continued well.

[15.3.46. Dr. Jobson reports that both these cases relapsed a month later.]

H. V. Forster said he would like to hear opinions as to whether penicillin should be used prophylactically before performing even conservative intranasal operations in cases of advanced pansinusitis? Post-operative complications were rare after these procedures in E.N.T. work but he had seen two or three cases of osteomyelitis of the upper maxilla with involvement of the ascending nasal process and the hard palate as sequelæ. Were they to do an extensive and mutilating operation in an attempt to save life, or would penicillin now come to the rescue? Would Mr. Hall or any other member who had treated such a desperate case kindly offer their advice?

A. W. McCay mentioned the case of a patient who had a chronic infection of her left antrum on which an intranasal antrostomy was performed. Ten days later she was readmitted to the hospital with a spreading osteomyelitis of the left maxilla. An extensive Caldwell-Luc operation was performed and the patient put on penicillin, in all one million units were given and this was combined with large doses of sulphathiazole. He was glad to say she made a complete recovery. He also mentioned a case of cavernous sinus thrombosis in a boy of 16 who made a complete recovery with the same treatment.

CONCLUSION

We consider that the treatment of tonsillectomy patients by penicillin pastilles is of value. The results are not dramatic but there is a reduction in the amount of exudate formed in the tonsillar beds and of the surface slough. This results in less scarring and, on the whole, the immediate post-operative symptoms are less marked. We consider that the best method is to start the penicillin treatment twenty-four hours before operation and to continue it for five days at three-hourly intervals, recommencing treatment as soon as the patient recovers from the anaesthetic. We found that if the penicillin pastilles are made with an agar base, a two-hourly interval is too short to allow the pastille to dissolve completely, whilst if the interval is increased to four-hourly, we think a sufficient concentration of penicillin is not maintained.

R. G. Macbeth: The investigations now proceeding were made in order to see how penicillin might be used in the ordinary cases of infection in laryngology and in rhinology. To do this three methods have been employed in cases of the ordinary type. First we tried the suction displacement method using 250 or 500 units of penicillin per c.c. as the lotion. Secondly we tried an emulsion made up with lanette wax containing 400 units per gramme, which was injected into the antrum in the acute or subacute or chronic cases and left in for a week. Thirdly we tried the effect of systemic penicillin in a few chronic cases.

Suction displacement was peculiarly successful in clearing up residual ethmoiditis after acute infections. In acute cases of infection of the frontal sinus or antrum the method has proved disappointing. All these cases have been bacteriologically controlled. The acute cases have done very much better than the chronic cases. The emulsion was injected through a wide cannula in amounts varying from 5 to 8 c.c., depending upon the size of the patient. At the end of the week the wash-out was done again, and any of the emulsion remaining which had been yellow when it went in was now colourless. The culture might still be positive, but the pus was much less in amount and might even have disappeared. In the chronic cases, on the other hand, this line of treatment has proved disappointing and almost all the cases have come to operation sooner or later.

The systemic application of penicillin has not been given deliberately to an uncomplicated acute case, but it has been observed that where the more serious complications were present, such as meningitis, provided the sinuses were in fact draining, the sinusitis cleared up well. This has been confirmed both by bacteriological control and by X-rays. Chronic cases have proved uniformly disappointing.

One type of case in which great temporary benefit has been obtained is atrophic rhinitis. The bacteriological picture was usually a mixed one, with staphylococci, diphtheroids and coliform organisms, but with the use of soaks or suction displacement the Gram-positive organisms disappeared. They are liable to recur, however, with undiminished vigour on cessation of treatment.

Penicillin is very valuable when given prophylactically after major operations upon the larynx and pharynx. Its use has reduced post-operative sepsis in such cases almost to vanishing point.

The President congratulated the openers of the discussion on bringing forward their results with judgment and not too much enthusiasm concerning a drug which had, unfortunately, been boosted so much in the Press; whereas penicillin, as Mr. Simson Hall had stated, was no substitute for surgery but an ideal adjunct.

His early experience of penicillin was not a very happy one. Within a period of six weeks he had seen and treated four cases of osteomyelitis of the frontal, referred to him after operation in other hospitals. They were all treated with penicillin. In each case the frontal sinus was opened radically but not obliterated. In the first case the osteomyelitis apparently cleared satisfactorily but, unfortunately, the patient was not X-rayed before leaving hospital. Six weeks later she reported back and while waiting to be seen developed an acute headache and died within one hour. The second case had an identical history, cleared up in the same way and exactly six weeks later complained of headache and died within an hour. In both cases an abscess had developed and burst into the frontal lobe. With the experience of these first two cases the third case was X-rayed at intervals. An abscess developed silently and was opened through the posterior wall of the frontal, the patient making a perfect recovery. The fourth case cleared up satisfactorily.

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In another case, a child of 7, on whom double antrotomy was done, all sorts of washings were carried out, but no form of irrigation seemed to make any difference. The child was then given only topical treatment with penicillin. She showed no improvement whatever for two weeks, still having a great deal of dirty slough, and then suddenly she changed, and the wash-out became perfectly clear. She had continued well.

[15.3.46. Dr. Jobson reports that both these cases relapsed a month later.]

H. V. Forster said he would like to hear opinions as to whether penicillin should be used prophylactically before performing even conservative intranasal operations in cases of advanced pansinusitis? Post-operative complications were rare after these procedures in E.N.T. work but he had seen two or three cases of osteomyelitis of the upper maxilla with involvement of the ascending nasal process and the hard palate as sequelæ. Were they to do an extensive and mutilating operation in an attempt to save life, or would penicillin now come to the rescue? Would Mr. Hall or any other member who had treated such a desperate case kindly offer their advice?

A. W. McCay mentioned the case of a patient who had a chronic infection of her left antrum on which an intranasal antrotomy was performed. Ten days later she was readmitted to the hospital with a spreading osteomyelitis of the left maxilla. An extensive Caldwell-Luc operation was performed and the patient put on penicillin, in all one million units were given and this was combined with large doses of sulphathiazole. He was glad to say she made a complete recovery. He also mentioned a case of cavernous sinus thrombosis in a boy of 16 who made a complete recovery with the same treatment.

Mr. J. F. Simpson said that he had recently had a case of maxillary sinusitis which even after a bilateral Caldwell-Luc operation still had a foul discharge. Culture showed a proteus and pyocyanous infection. Under the combined treatment of penicillin and a 2% solution of phenoxetol applied locally the case had done very well, the previous yellow foul discharge completely disappearing.

I. Simson Hall, in reply, said that on the question of prophylactic penicillin, except with regard to such simple administrations as lozenges or snuff, he thought there was no case made out for any such drastic treatment. It was not wise or useful to push needles into people just in the hope of curing the exceptional case which might occur two or three times only in one's professional life.

R. H. Hunt Williams said that the frontal sinusitis case he had shown, in which a ureteric catheter had been used, had a pyocyanous infection which was apparently cleared up with phenoxetol.

J. F. O. Mitchell, also in reply, said that on the question of penicillin mists, when they were considering starting the series of cases he had mentioned in his paper, they debated whether solution or snuff would be better. They decided that when a snuff was inhaled it followed the course of the inspired air, adhering to the mucous membrane and giving a higher and more lasting concentration, and in view of this and of the fact that it was much handier for the treatment of the ambulant patient, they decided that the use of snuff would be better than solution or very fine mist. Penicillin lozenges alone were of very little use in cases of follicular tonsillitis because the penicillin did not penetrate into the depth of the crypt. In such cases he used sulphonamides systemically and penicillin locally.

E. G. Collins said that he could not presume to answer a question which had been asked as to the potency of certain penicillin preparations. But in the case of the Burroughs Wellcome lozenges the potency of penicillin in the lozenge had been tested. It was a bacteriological test and there proved to be very little deterioration with keeping.

Section of Psychiatry

President—G. W. B. JAMES, C.B.E., M.C., M.D., D.P.M.

[January 8, 1946]

Personnel Selection: By Whom?

By ALEC RODGER

THE working population of this country consists of approximately twenty million persons. Nineteen millions of them are employees of somebody else and so have to go through some sort of personnel selection procedure at least once in their lives. Many have to go through the process many times; for example, when they are seeking to change their employer, or when they are applying for promotion or transfer under the same employer.

The amount of personnel selection work to be done is therefore enormous. And relatively little of it is being tackled by really sound methods. In the circumstances, it is not surprising that people with Service personnel selection experience, acquired mainly during the recent war, have been thinking a great deal about the application of that experience to civil life. But it is surprising, I suggest, and even a little alarming, that some among them seem prepared to model their plans very closely indeed on those adopted by the Services, and to advocate schemes which would involve a vast amount of centralized, or at least regionalized, personnel selection.

I want to propose a substitute for these schemes. Let me start off with three facts:

First, vital though personnel selection often seems to those of us who are engaged upon it, it is not widely regarded as a particularly important activity. In an ordinary industrial or commercial undertaking, personnel selection is only one function of several carried out by the personnel department; and the personnel department itself is not always "on the top line". The Chief Inspector of Factories, in his Report for 1943, gave the results of an analysis of the position occupied by the heads of personnel departments in factories. In 30% the senior officer was found to be responsible to the managing director; in 21% to another director; in 46% to the works manager; and in 3% to the works engineer or the secretary of the company. Thus, in about half the factories the head of the personnel department had no uninterrupted approach to the board room.

Secondly, the great majority of employing organizations in this country are very small. About 90% of them employ fewer than 250 people. For most of them, therefore, personnel selection is an occasional affair. But it is one which they tend to regard as very much their own concern. Maybe times will change, but it is worth remarking that at present my point holds good of quite large organizations, because most of them allow a high degree of autonomy to their constituent companies and do not usually centralize their personnel selection work, except when they are handling the appointment of senior executives.

Thirdly, for certain large groups of workers, mainly of the machine-operator kind, comprising about a quarter of the gainfully employed, personnel selection is becoming decreasingly important. Considerable attention is being devoted nowadays, by industrial psychologists and others, to what is sometimes called "work-simplification", through improvements in the design and lay-out of equipment, in methods of work, and in methods of training for work. All this is tending to make more and more employments fall within the competence of a larger and larger proportion of the working population.

I have mentioned these three facts, because they must be taken into account, if our discussion of civilian personnel selection problems is to be realistic. We must recognize that, although the field is enormous, it is not generally held to be of first-rate importance; it is split up into little pieces which cannot easily be made into one large piece, or even into several fairly large pieces; and parts of it are decreasing in significance.

But, it may be asked, isn't this a strangely pessimistic argument? Why shouldn't the Ministry of Labour and National Service use its now powerful position to urge the importance of personnel selection, and why shouldn't it decide to offer a personnel selection service to employers? I hope the Ministry will urge, constantly, the importance of personnel selection; but, both as an industrial psychologist and as a private citizen, I hope it will resist the coaxing of those who want it to undertake personnel selection duties on behalf of employers. As an industrial psychologist, I doubt whether the Ministry could be expected to compete with the task, unless it possessed a large army of specially trained technicians. As a private citizen, I think that any such arrangement would rightly be regarded as undesirable. Certainly, the job of making it compatible with the doctrine of "freedom of choice of employment" would be a tricky one.

It may be suggested, however, that the rejection of a centralized or regionalized industrial personnel selection scheme would throw on to employers too much responsibility for seeing that misfits were avoided. I doubt whether it would. It seems to me that the real solution of this problem lies in the development, by the Ministry of Labour and National Service, aided by the Ministry of Education, of a first-rate vocational guidance system. Personnel selection is in practice an employer's approach to the "round-peg" problem. In vocational guidance we have the approach of the private person, who comes along not as a candidate for a particular vacancy but as an individual seeking advice. If the Ministry of Labour were able to strengthen still further its present vocational guidance schemes for young people and adults, and to ensure that employers were only rarely faced with really unsuitable candidates, whose unsuitability they found it hard to detect, industry's personnel selection problem would be much nearer solution. Broadly, then, I would say: Let us press for the development of official vocational guidance rather than for the development of official personnel selection. (There must, of course, be official personnel selection for Government jobs.)

To all this, however, I must add three comments: First, the successful working of any such plan would involve the Ministry of Labour in the arrangement of thorough training courses for carefully selected advisory officers, and in the arrangement of a scheme whereby these advisory officers were able to keep in frequent and regular touch with each other and with the people who had trained them. I realize that this is more easily proposed than put into practice, partly because it raises difficult questions—difficult from the point of view of the Treasury—about the extent to which civil servants in certain classes should be permitted to become specialists; but I cannot see any other way of tackling the problem. Personally, as I indicated to the Hankey Committee on Higher Appointments two years ago, I would like the Ministry to set up centrally a model Appointments Office, Local Office and Juvenile Employment Office, which would serve as a composite training unit for its interviewing staff. This unit, which would train people "on the job", might have the assistance of both psychiatrists and industrial psychologists, and of any others—for example, economists—whose help might be useful.

Provided there were available a really good system of post-training supervision, the training course itself need not last more than three months. I am not hopeful of anything satisfactory being done under that time. Before the war, new members of the vocational guidance staff of the National Institute of Industrial Psychology were not generally permitted to send out reports on their own responsibility until they had spent about a year there. I must admit, however, that we were dealing almost exclusively with the vocational guidance problems of young people of what might be called Appointments Office level; that is, they were mostly the moderately able sons and daughters of the relatively well-to-do. I must admit, too, that we were trying to produce written reports which would, to a sufficient extent, stand up to the criticism not only of our victims but also, sometimes, of their parents, headmasters, family solicitors and family doctors, and occasionally of psychiatrists and Ministry of Labour officials. All this made us rather careful, and it is probable that with more thorough organization and less concern for the views of our many potential critics we could have cut down that basic training period.

But of one thing I am quite certain, and that is that the art of vocational guidance cannot be taught in short courses which consist of lectures with no—or hardly any—practical work. Possibly such courses have some use as a sort of "first aid" arrangement, but that is scarcely what is needed. I emphasize this point, because on a number of occasions during the past few years I have had to meet, in some way, requests for lectures and discussions from people who are quite certain that industrial psychologists (and psychiatrists, too) can give all the instruction they need to give through one or two lectures.

And now for my second comment on the development of the Ministry's vocational guidance service. It is evident from pre-war vocational guidance experience, and from wartime personnel selection experience, that a considerable measure of sound self-guidance and self-selection can be stimulated by the provision of relevant information about occupations. When the Royal Navy's present personnel selection scheme was instituted, in the summer of 1941, a cue was taken from the vocational guidance work of the NIIP, and stress was laid on the desirability of providing candidates with an "information service" about naval employments. At the Combined Recruiting Centre stage, a simple descriptive leaflet was made available to them before they had their interview with the Naval Recruiter. (In fact, through the co-operation of the Ministry of Labour it was sent out some days in advance to all men and youths, called up under the Armed Forces Act, who had at the time of their registration expressed a preference for the Navy.) In the Entry Establishments, where the further allocation of recruits was carried out, information about the jobs available was purveyed by means of informal

lectures, by posters and photographs, and occasionally by films and displays of equipment. In these ways new entries to the Service were given some appreciation of the duties involved in the various branches, and of the qualifications required for entry to them and progress in them. The self-selection thereby introduced contributed quite substantially, I am sure, to the success of the whole personnel selection scheme.

My third comment must be on the importance of a point of economics. We have all been made aware of the necessity for an enormous increase in our export trade. But the working population is shrinking, not only because of the fallen birth-rate are coming upon us but also because the 1944 Education Act will—over a period of a few years—result in the delayed entry of hundreds of thousands of young people to the labour market. It will no doubt be difficult for us to escape “direction” of some sort. Presumably we shall seek to have our peacetime direction done for the most part by economic rather than legal sanctions; that is, by the manipulation of wages rather than by telling people exactly where they must go and what they must do. I suggest that a planned wage structure for the whole of industry, aided by a sound vocational guidance scheme, for adults as well as juveniles, and supported by a really good, well-balanced “information service” about the employments available, might gain for us most of the advantages of a less palatable system.

But, obviously, even with the best vocational guidance scheme imaginable, there will still be a need for personnel selection by employers. How should this be done? So far as the bulk of the personnel selection work is concerned, the answer is, I suggest, fairly clear. It should be carried out by suitable members of a firm's personnel department who have received appropriate training in interviewing, in record-keeping (a very important matter) and in the use of any selection tests which may be judged suitable. The experience of the NIIP suggests that this training can most economically be given in short courses of lecture-discussions and demonstrations, organized for groups of people at some central place, followed by individual practical work on the home-ground of each of the firms represented. This arrangement for the practical work is very desirable, in order that at least one of the lecturers might have an opportunity of acquainting himself with the particular nature of the firm's selection problems. It is desirable, too, that this same lecturer should be able to continue his tuition through occasional visits, and that he should be in a position to provide his students with good notes. (And among these I personally would include, until something more appropriate becomes available, a copy of a booklet which is now part of the equipment of Personnel Selection Officers in the Royal Navy. It is called *An Employee Evaluation Manual for Interviewers*, and it is published by the Psychological Corporation of New York.)

Let us take up separately the problem of selecting personnel for senior appointments or for some form of advanced training. To what extent can we expect industry to adopt methods similar to those thrashed out during the past four years by the War Office Selection Boards? The Civil Service Commissioners have set the pace. It is true that they have departed from orthodoxy, as the Admiralty did before them, by employing industrial psychologists in place of psychiatrists plus educational psychologists; but their pattern is the same. Is industry likely to follow their example? My guess is based on limited knowledge, but it is that progress in this direction will be slow. I know that some employers believe, rightly or wrongly, that the institution of a WOSB scheme for selecting candidates for their higher appointments would frighten off some very suitable ones. There is, I suspect, more chance of WOSB methods being used in selection for the professions, and I imagine that those who have been concerned with WOSB research and training will have explored fairly thoroughly the prospect of tackling the medical and teaching professions particularly. They are, presumably, the ones which should be most responsive. But it is rather saddening to reflect that, although the teaching profession is faced with a problem not unlike that faced by the Service departments in regard to officer-selection, nothing appears to have happened yet. This can scarcely be due altogether to anxiety about numbers, which might lead to a fear on the part of the authorities that they will have to take practically everyone who applies, because it has been made known that the present rejection rate from the ordinary boards is about 50%. The only professional group which seems to show signs of progressiveness in this matter consists of the clergy. The Anglican Church, both at home and abroad, has at least adopted the plan of having a well-organized selection “conference”, lasting a few days, at which candidates for ordination are put on trial.

In the selection of executives for industry, there is much to be said for the method developed in pre-war years by the NIIP, whereby a firm's usual selection procedure—the completion of an application form, followed by one or two interviews—was tidied up and supplemented by testing and interviewing carried out by one or two members of the National Institute's staff. I have described and discussed this in another paper, and

I will not trouble you with the details, but I want to say that it appeared to work to the satisfaction of the firms concerned. It was a one-day procedure. A group of eight or nine short-listed candidates presented themselves at the National Institute's headquarters. They were given a short explanation of the procedure and were then—as a group—put through appropriate written tests. These, and the completion of a biographical questionnaire, took up most of the morning. After an early lunch, they were interviewed, usually by two members of the NIIP staff sitting separately. The interviews normally lasted from twenty to twenty-five minutes each. By tea-time the interviewers had finished their interviews and were able to sit down to a discussion of the relative merits of the candidates and to the preparation of a short written report. This report was offered to the firm as the technical advice of an independent assessor. The final decisions were made by the firm after consideration of the report. Sometimes a representative of the National Institute was present when the company's decisions were made; more often he was not.

A good deal of work along similar lines has been done for the Royal Navy and the Royal Indian Navy in the field of officer-selection, for the Admiralty's modification of WOSB techniques has been applied only to certain large groups of officer-candidates. A penetrating discussion of it has been provided by my former colleague, Dr. N. A. B. Wilson, in a paper recently published by the NIIP. It is called "Interviewing Candidates for Technical Appointments or Training".

At this point I want to make a short comment on the relationship between psychiatrists and industrial psychologists in regard to work of this kind. For a number of reasons, including the hard fact that both psychiatrists and industrial psychologists are scarce and must almost inevitably handle a wide variety of problems, I believe that attempts to define very clearly the responsibilities of both in the personnel selection field are at present likely to be unprofitable. What is now greatly needed in the civilian sphere is the sort of intermingling which has taken place on the War Office Selection Boards, and I am quite sure that the NIIP will do its utmost to foster co-operation, not only between psychiatrists and industrial psychologists, but between both of them and other scientific workers. Before the war we had, at the National Institute, a loose but effective liaison with the Tavistock Clinic in our consulting work, and one survey of our records showed that one in every ten of those who sought vocational guidance had been advised to see a psychiatrist before making a definite choice of occupation. (The proportion among the adult applicants was a little higher, because—as one would expect—this group included a larger proportion with schizoid tendencies.) I would like to see that link strengthened appreciably by the participation of psychiatrists in the National Institute's teaching work and in its investigations in industrial organizations.

SUMMARY

First, there is clearly a great deal of personnel selection work to be done, and for several reasons it would be absurd to suggest that psychiatrists and industrial psychologists should have a direct hand in all of it. I suggest that their main function should be to help in the technical training and supervision of the non-technicians who will assuredly continue to do most of it; and of course to give assistance in the necessary research work.

Secondly, there is, in my judgment, a part to be played by both psychiatrists and industrial psychologists in the actual selection of certain groups of people, particularly for the professions and senior appointments in industry. We should not yet attempt to define very rigidly their special responsibilities; but they should both stand in a technical-advisory relationship to the employers who consult them.

Thirdly, I think it would be very unfortunate if the Ministry of Labour, or any other central organization, were persuaded to provide a personnel selection service for employers. I believe that the Ministry should aim at easing industry's personnel selection problem by the further improvement of its vocational guidance arrangements. Most of the advantages of a centralized personnel selection system might be gained by the building-up of a really good vocational guidance scheme for both young people and adults, provided that there was available also a first-rate "information service" about occupations, and provided also that we were able to work steadily—and not too slowly—towards a planned wage structure for the whole of industry. In any case, personnel selection is bound to be a negative process for those who are rejected; from the individual's point of view, vocational guidance offers a positive approach to the problem.

Fourthly, and lastly, in this vocational guidance field, as in the field of personnel selection, there is a need for both psychiatrists and industrial psychologists, not only to give assistance in the training of the vocational guidance staffs of the Ministry of Labour and certain Local Education Authorities, but also to take part in research. And, of course, if we are to make technical progress, psychiatrists and industrial psychologists must have opportunities, either official or private, for giving vocational guidance themselves.

Section of Pathology

President—Professor W. G. BARNARD, F.R.C.P.

[December 18, 1945]

DISCUSSION ON THE TOXÆMIA OF GAS GANGRENE

Mr. F. A. R. Stammers: *The surgical aspects of gas gangrene.*—Gas gangrene has long been recognized as a specific infection of devitalized muscle but it is much more important to appreciate it as a disease of circumstances. It is to the tremendous importance of these circumstances in relation to the incidence and mortality of gas gangrene that I wish to call particular attention.

Reference to the History of World War No. 1 shows that although almost nothing was known of the disease before 1914 yet much accurate knowledge was accumulated during the next two years. I will quote from it a few extracts from reports from surgeons such as Grey, Frankau and Wallace, and from pathologists such as Shaw Dunn and McNee: "Pieces of clothing carried in by shell fragments were responsible for a very large number of cases." "The disease was in the main an affection of the muscles." "The disease could in most cases be cut short by excision of muscles." "Defective blood supply is the principal cause."

The circumstances of surgery in war.—War surgery is different from any other kind of surgery, not because the soldier reacts to trauma differently from the civilian but because the circumstances under which he is wounded and under which the surgeon has to treat him are peculiar. What is right for the desert may be wrong in cultivated countries; what is possible in static warfare may be unattainable or dangerous in a war of movement; the case of six hours' standing can be treated differently from the one wounded three days previously. To put it in another way, compare the man fighting in the relatively sterile sand of the desert, dressed in shorts and an open shirt and exposed to sun, with his comrade fighting over the highly cultivated soil of North Africa and Sicily during the cold and wet winter months, his six or eight thicknesses of clothing soaked with heavily infected liquid mud; or the man in open country wounded cleanly by a sniper's bullet, with the man with his foot blown off and his calf muscles shredded up to the knee-joint through stepping on a schu-mine.

Etiology.—Gas gangrene is an infection of devitalized muscle by gas-forming organisms, though fascia, blood-clot and brain are also susceptible. The mere presence of clostridia in a wound is not sufficient—the damaged muscle is the essential thing, and major muscle wounds such as those of the buttock, thigh, calf and scapulo-axillary regions are especially liable to gas infection. Missiles such as jagged pieces of shell, mine and mortar cause more disruption of tissue than do bullets, and indriven pieces of dirty clothing or equipment are especially lethal. Anything affecting the blood supply, either directly or indirectly, encourages the disease. Thus injury to blood-vessels, tourniquets, tight bandaging, badly applied splints and ambulance journeys over rough roads all embarrass the blood supply, but the general lowering of blood-pressure resulting from hæmorrhage, shock, dehydration, exposure to wet and cold further contributes to the liability to gas gangrene. Of special significance is the observation from all fronts that something is absorbed from damaged muscle that leads to a prolonged lowering of blood-pressure, which latter will encourage gas gangrene if clostridia be present. There is a close resemblance between the case of gas gangrene toxæmia and the case of absorption of the products of lacerated muscle. Macfarlane and MacLennan in January of this year made an interim report suggesting that part of the syndrome of gas gangrene toxæmia was indeed due to the absorption of the products of breakdown of muscle resulting from clostridial infection of it.

Time is another important factor. It has been shown repeatedly that infection in wounds remains relatively superficial for the first eight to twelve hours but that after this time the deeper tissues become involved. Delay in applying surgical treatment until after this optimum interval encourages sepsis, including the risk of gas gangrene.

Symptoms and signs.—From the surgical point of view gas gangrene may present itself either as an established case (as for instance in men who could not be rescued for many hours), as an unexpected finding at first operation, or as a complication developing after the first operation—latterly a very rare event. Cases whose collection has been inevitably delayed were sometimes admitted prostrated, with cold, blue, clammy extremities, a running pulse, the wounded part being painful, swollen, livid or mottled and becoming plum-coloured from hæmelysis. Gas might or might not be present; it could often be detected with varying pressure of the stethoscope earlier or more

readily than with the fingers. If muscle was exposed it was dry and dull, and discharges were no more than an evil-smelling thin fluid. Sometimes jaundice developed.

In the case discovered unexpectedly at operation one or two affected muscles of a group, or part only of one muscle belly, with clear demarcation between normal and abnormal, are discovered during exploration of the wound. The affected muscles may be salmon pink or red, and only in extreme cases black and diffuent, and in any case they do not contract or bleed when cut. The surrounding tissues may be normal or distended with yellow œdema, and fine gas bubbles may be seen in both muscle and intermuscular septa.

In the case developing after operation the onset is sudden. There is local pain, malaise, rising temperature and pulse, and sometimes vomiting, but the outstanding and most characteristic thing is the toxæmia. From a relatively normal individual he will within an hour or so become anxious, euphoric, or wildly excited, and the pulse rapidly deteriorates. Such a case is near the end, and may turn over to reach for a drink and fall back dead in the very act. In the earlier days of the war much importance was attached to the significance of the development of pain, but during the last twelve months in Italy several surgeons remarked on the absence of pain—probably the result of better and earlier surgery, aided by penicillin.

Rather less than 50% of cases actually develop gas. One warning is called for since in the past unnecessary amputations have been performed because of the presence of emphysema. It has to be remembered that muscle fibres, cut by a sharp fragment of metal, spring apart and, like the piston of a syringe, may suck air through the skin wound into the gap. This rapidly becomes disseminated and by the inexperienced may be diagnosed as gas. The absence of toxæmia should obviate this error.

Treatment.—The essentials of treatment are surgery, blood and other intravenous fluids, and antitoxin. Generous skin incisions are needed for adequate exploration of the depth of the wound. Foreign matter, especially pieces of clothing or equipment, must be sought for and removed, and all affected muscle excised. It is best to do this by removing the complete muscle belly from origin to insertion, though in large muscles like the adductor magnus it may only be necessary to remove one part of it. All discoloured muscle and all muscle that does not bleed or contract under the knife should be removed. The deep fascia is incised longitudinally and transversely for decompression and drainage. The wound is then heavily frosted with penicillin powder and the skin is left open, being dressed with a layer of dry gauze. Enormous amounts of muscle may have to be removed—I have thrice seen all the gluteal muscles removed, with survival in two cases—and a limb may be so disorganized as to require immediate amputation, but the amputation rate is much less since better prophylactic surgery has been universally applied. These patients are always short of fluids and blood, but as the need for surgery is urgent too much time should not be spent on resuscitation: put in two pints rapidly and then take the case to the theatre with the drip still running. At the end of operation inject 100,000 units antitoxin. The intravenous drip should be continued for several days, an average of five pints daily being given. This should include one bottle of plasma daily to replenish protein and blood should be given according to hæmoglobin observations. All our forward units had a van Slyke's copper sulphate set and we always gave 15,000 units of penicillin three-hourly for about three to seven days, and although I am not at all convinced that it affected the clostridial infection I am sure that it prevented a staphylococcal infection.

I am strongly of the opinion that the treatment of gas gangrene is preventive, and by foreseeing and circumventing the adverse factors in the particular circumstances of the moment I believe that the disease can be almost eliminated. It becomes therefore a matter of organization as much as of surgical technique, and our policy in Italy was as follows:

(1) Surgical centres were so deployed that under all circumstances there was a reasonable chance that every major case would receive surgical treatment within two to six hours of wounding, and all the remainder within twelve hours. In busy centres extra surgical teams would be added. Where roads were blocked or where a minor axis was relatively isolated a Field Surgical Unit would be sent forward to work with a Field Ambulance, with instructions to operate on life-threatening conditions only—this included major muscle wounds.

(2) At the earliest possible moment all major wounds were given sufficient antitoxin to contain 8,000 units of anti-*Cl. welchii*. This was given routinely at the Advanced Dressing Station, but where evacuation to this was likely to be delayed—as in the mountains north of Florence—the antitoxin was issued to the Regimental Aid Posts.

(3) All major muscle wounds—calf, thigh, buttock and scapulo-axillary region—

were regarded as top priority cases, but even small muscle wounds were treated by careful excision too.

(4) Muscle wounds were carefully splinted at the earliest moment practicable.

(5) Because of the effect on blood-pressure of massive injury to muscle of over three hours' standing too much time was not spent on resuscitation—surgical intervention was considered the essential thing.

(6) The surgical treatment of wounds has already been described.

Dr. J. D. MacLennan: The Oxford English Dictionary defines toxæmia as a "morbid condition of the blood, caused by a toxin", and a toxin as "a specific poison, especially one produced by a microbe", and few who have watched a man die of gas gangrene can have had any doubts that these definitions were correct, and that here, in a most extreme and literal sense, was an example of bacterial blood poisoning. The fact that specific anti-sera have been shown to be of very great value in treatment lends considerable weight to this theory.

Now, at first glance, there seems to be such an overwhelming body of evidence in favour of such a view that it would be not only futile but even a little presumptuous to criticize it. Nevertheless, some recent observations which Dr. R. G. Macfarlane and I have made in the field have provided grounds for doubting whether the pathological process in man is so simple as is generally believed, whether indeed bacterial toxins as such are circulating, at all. It is this new information that I should like to bring forward.

Of the organisms causing gas gangrene in man *Cl. welchii* is by far the most important, and it is with *Cl. welchii* infections that I shall deal. As you are aware, this organism produces a whole devil's brew of toxins, and different varieties and subspecies of Welch bacillus have been described, each producing different toxins or different combinations of the same toxins. Although some of these toxins are poorly defined, and others are almost certainly still awaiting recognition, I do not think there can be any reasonable doubt that, so far as the local lesion in gas gangrene is concerned, the alpha-toxin is the component of prime importance. There is a very large volume of evidence in favour of this which need not be reviewed here, but I should particularly like to mention the recent work of Evans and of Robb-Smith. Doubtless others of the many enzymes elaborated by *Cl. welchii* must also play their part in producing the intense necrosis and peculiar tissue reactions seen in gas gangrene, but theirs must almost certainly be subsidiary roles. In view of all this, it was therefore with considerable surprise that Macfarlane and I failed to identify the alpha-toxin in the infected tissues or wound exudates (still less the blood) of 24 cases of gas gangrene due to *Cl. welchii*. It is true that in 3 cases we obtained some slight evidence of the presence of a lecithinase after twenty-four hours' incubation, but these were cases in which the tissues had been obtained post mortem and, as we have reason to believe, in these the lecithinase was produced by the multiplication of the Welch bacillus in the tissues after death.

Moreover, for reasons which we have set out in detail elsewhere, it seems improbable that these negative findings can be attributed solely to the presence of antitoxin or of phosphates, and we are forced to the conclusion that the alpha-toxin is not released into the exudates and tissue-fluids during life, because it is at once fixed by living tissues. We have not as yet been able to show that this occurs in man, but we have some evidence of its occurrence in animals (MacLennan and Macfarlane, 1945; Macfarlane and MacLennan, 1945).

It might of course be argued that the alpha-toxin is at once carried away in the blood-stream, but such experiments as we have been able to undertake are not in favour of this. First of all, we tried giving repeated small doses of toxin intravenously to rabbits, in an attempt to produce the slow absorption from infected muscle. The effect of these doses was, in every case, the appearance of intravascular hæmolysis and hæmoglobinuria. If the total dosage was sufficiently small, this hæmolysis was the only ill-effect observed. If a lethal dose was given the animal died with more or less complete intravascular hæmolysis. All these effects might be expected from the presence of a hæmolytic toxin in the blood-stream, and it is clear that given in this way, the minimum lethal dose is much larger than the minimum hæmolytic dose. When the toxic filtrate was injected intramuscularly, however, there were important differences in effects. No significant hæmolysis or hæmoglobinuria was observed, but the animal developed a fatal state of collapse and circulatory failure. The minimum lethal dose of toxin by this route, though larger than that required to kill when given intravenously, is not sufficient to produce hæmolysis.

In human gas gangrene the findings resemble those seen in rabbits injected intra-

readily than with the fingers. If muscle was exposed it was dry and dull, and discharges were no more than an evil-smelling thin fluid. Sometimes jaundice developed.

In the case discovered unexpectedly at operation one or two affected muscles of a group, or part only of one muscle belly, with clear demarcation between normal and abnormal, are discovered during exploration of the wound. The affected muscles may be salmon pink or red, and only in extreme cases black and diffident, and in any case they do not contract or bleed when cut. The surrounding tissues may be normal or distended with yellow œdema, and fine gas bubbles may be seen in both muscle and intermuscular septa.

In the case developing after operation the onset is sudden. There is local pain, malaise, rising temperature and pulse, and sometimes vomiting, but the outstanding and most characteristic thing is the toxæmia. From a relatively normal individual he will within an hour or so become anxious, euphoric, or wildly excited, and the pulse rapidly deteriorates. Such a case is near the end, and may turn over to reach for a drink and fall back dead in the very act. In the earlier days of the war much importance was attached to the significance of the development of pain, but during the last twelve months in Italy several surgeons remarked on the absence of pain—probably the result of better and earlier surgery, aided by penicillin.

Rather less than 50% of cases actually develop gas. One warning is called for since in the past unnecessary amputations have been performed because of the presence of emphysema. It has to be remembered that muscle fibres, cut by a sharp fragment of metal, spring apart and, like the piston of a syringe, may suck air through the skin wound into the gap. This rapidly becomes disseminated and by the inexperienced may be diagnosed as gas. The absence of toxæmia should obviate this error.

Treatment.—The essentials of treatment are surgery, blood and other intravenous fluids, and antitoxin. Generous skin incisions are needed for adequate exploration of the depth of the wound. Foreign matter, especially pieces of clothing or equipment, must be sought for and removed, and all affected muscle excised. It is best to do this by removing the complete muscle belly from origin to insertion, though in large muscles like the adductor magnus it may only be necessary to remove one part of it. All discoloured muscle and all muscle that does not bleed or contract under the knife should be removed. The deep fascia is incised longitudinally and transversely for decompression and drainage. The wound is then heavily frosted with penicillin powder and the skin is left open, being dressed with a layer of dry gauze. Enormous amounts of muscle may have to be removed—I have thrice seen all the gluteal muscles removed, with survival in two cases—and a limb may be so disorganized as to require immediate amputation, but the amputation rate is much less since better prophylactic surgery has been universally applied. These patients are always short of fluids and resuscitation: put in two pints rapidly and then take the case to the theatre with the drip still running. At the end of operation inject 100,000 units antitoxin. The intravenous drip should be continued for several days, an average of five pints daily being given. This should include one bottle of plasma daily to replenish protein and blood should be given according to hæmoglobin observations. All our forward units had a van Slyke's copper sulphate set and we always gave 15,000 units of penicillin three-hourly for about three to seven days, and although I am not at all convinced that it affected the clostridial infection I am sure that it prevented a staphylococcal infection.

I am strongly of the opinion that the treatment of gas gangrene is preventive, and by foreseeing and circumventing the adverse factors in the particular circumstances of the moment I believe that the disease can be almost eliminated. It becomes therefore a matter of organization as much as of surgical technique, and our policy in Italy was as follows:

(1) Surgical centres were so deployed that under all circumstances there was a reasonable chance that every major case would receive surgical treatment within two to six hours of wounding, and all the remainder within twelve hours. In busy centres extra surgical teams would be added. Where roads were blocked or where a minor axis was relatively isolated a Field Surgical Unit would be sent forward to work with a Field Ambulance, with instructions to operate on life-threatening conditions only—this included major muscle wounds.

(2) At the earliest possible moment all major wounds were given sufficient anti-toxin to contain 8,000 units of anti-*Cl. welchii*. This was given routinely at the Advanced Dressing Station, but where evacuation to this was likely to be delayed—as in the mountains north of Florence—the antitoxin was issued to the Regimental Aid Posts.

(3) All major muscle wounds—calf, thigh, buttock and scapulo-axillary region—

The statistical data obtained established in principle that the use of antitoxin gives a patient a better chance of recovery, but in the field antitoxin appears to be almost as essential as surgery for a good recovery rate. In the various campaigns of the British Army the recovery rate from gas gangrene ran parallel to the proportion of the cases receiving early and adequate treatment in addition to surgical treatment (MacLennan and Macfarlane, 1944). The rise in the mean recovery rate for all cases, from 30% in Sicily to 70 to 75% in the later stages of the Italian campaign and in the B.L.A., was substantially due to the wider and intensive use of antitoxin, and not simply to a general improvement in the conditions, or any attenuation of the disease; for the recovery rate amongst those receiving adequate antitoxin therapy showed a relatively slight improvement (from 65 to 75%) over the same period, in spite of better military conditions, experienced surgeons and the introduction of penicillin. The fact that with the best treatment possible the death-rate remained about 25% indicates, however, the existence of another cause of toxæmia in addition to the bacterial toxin (Macfarlane, 1945).

From the biochemical point of view, several causes of the toxæmia of gas gangrene seem possible. (1) *Action of the bacterial toxin on a vital organ: Cl. welchii* toxin contains a lecithinase which is probably identical with the alpha-toxin (Macfarlane and Knight, 1941). The interest of this enzyme lies in the physiological significance of lecithin, particularly in relation to the permeability of the cell membrane. From analysis of different fractions of rabbit muscle it appears that lecithin is associated with myosin, the contractile protein in the fibril, as well as with the sarcolemma. It seems possible that the fibril is invested with a lipid layer which prevents the diffusion from the fibril of substances, such as adenosine-triphosphate and phosphocreatine, necessary for the cycle of contraction, and that it is the destruction of this layer by the bacterial lecithinase which leads to the uniform staining of the fibril and the early loss of contractility noted by McNee and Shaw Dunn (1917). Toxæmia or death may therefore be due to the loss of contractility of cardiac muscle, before any gross change in the heart is visible. (2) *Production of a toxic substance by infecting organisms*: So long as infected tissue remains in the body, the possibility that the toxæmia is due in part to immunologically non-specific substances must be borne in mind. *Cl. welchii*, for instance, produces histamine from histidine, so that the conjunction of this organism with a proteolytic organism might give a different picture from that in an experimental infection with *Cl. welchii* alone. (3) *Toxæmia due to ischæmic muscle*: In a large proportion of the cases, gas gangrene arose in muscles with a damaged blood supply; in addition, traumatic or hæmorrhagic shock sustained at the time of the injury presumably contributes to an anoxæmia which causes further tissue damage. After the occurrence of renal failure, similar to that seen in the crush syndrome, had been reported (Jeffrey and Scott Thomson, 1944) some biochemical investigations on the nature of this toxæmia were planned. Specimens of muscle from cases of gas gangrene and of vascular gangrene amongst the B.L.A. casualties were received from Major MacLennan; comparison of the chemical analyses with that of normal muscle showed that both in the gangrenous and in ischæmic muscle a marked loss of adenyly compounds, creatine and potassium had taken place. The loss of potassium is of interest in view of Rosenthal's work on the electrolyte balance in experimental shock, and the fact that, in incipient shock, the lethal dose of potassium is decreased to about one-eighth of the normal dose (Tabor and Rosenthal, 1945). It seems very probable that local changes due to an increased permeability of the cell membrane, whether caused by the bacterial toxin or by anoxæmia, play an important part in the development of the toxæmia of gas gangrene.

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Sir Percival Hartley and Dr. D. G. Evans: As a result of the war, the Department of Biological Standards at the National Institute for Medical Research, Hampstead, became responsible for the supply of the international standards for the gas gangrene antitoxins (Hartley, 1945). Two of these had originally been prepared at Hampstead (Hartley, 1931; Hartley and Bruce White, 1935) and replacement standards for three of them were made during the war (Hartley and Evans, 1942 '3). Shortly after the outbreak of war doubts were expressed as to the adequacy of the international standard for *Cl. welchii* Type A antiserum; it was argued that while the standard provided for the assay of a antitoxin other activities of the organism, such as its power to produce hæmolysin and hyaluronidase, and the bearing of these on infection and of the corresponding antibodies in the

muscularly, rather than in those injected intravenously. Even in rapidly fatal cases, who have received no antitoxin, it is exceptional to observe hæmoglobinæmia or hæmoglobinuria. Indeed, throughout the whole war, I have myself seen only 3 such cases and know of a total of not more than 7. All appear to have been associated with a true *Cl. welchii* septicæmia.

The question at once arises, what is this toxic factor? There seem to be two main possibilities. It may be that the traditional view is correct and that bacterial toxins are seeping into the circulation from the infected tissues, perhaps even the alpha-toxin itself; for it is conceivable that if it reaches the blood-stream in small amounts it might not cause obvious hæmolysis, and yet by localizing in vital centres—the C.N.S. is particularly rich in lecithins for example—gradually build up a concentration sufficient to cause irreparable cell-damage. Indeed, if a bacterial toxin is involved, it seems most likely to be the alpha-toxin, for both the experimental work and the clinical experience of this war have shown that the value of *Cl. welchii* therapeutic antiserum lies primarily in its anti-alpha-toxin content.

There is, however, one serious drawback to this view. Experimentally we have shown that in adequate dosage *Cl. welchii* anti-serum will protect rabbits from the intravenous inoculation of lethal doses of *Cl. welchii* filtrate, but this is certainly not always true of the natural muscle infection. We made antitoxin titrations in 28 cases of gas gangrene, and found that the presence of an excess of antitoxin in the blood-stream and wound area will not necessarily prevent a fatal outcome. Moreover, the only fatal cases in this series were those in whom the surgeons had failed to remove all the infected tissue; and this at once suggests the second, and to me attractive possibility, that a non-hæmolytic toxic factor, not neutralized by antitoxin, may be derived from disintegrating muscle.

The implications of such a theory are obvious—it would link up the shock-like prostration of gas gangrene with the very similar condition resulting from severe trauma, and possibly also with the crush-syndrome and related states.

In conclusion I should like to stress one point. It has been suggested that these latest findings of ours make clear the worthlessness of serum treatment in gas gangrene. Nothing could be further from the facts. Personally, having dealt with little else than gas gangrene and related conditions for the active period of the war, I have not the slightest doubt of the value of antiserum both in prophylaxis and treatment. When I first saw large numbers of cases in 1940, our mortality rate was well over 50%—since 1942 (apart from a bad patch in Sicily) it has been below 30% and all the evidence relates this considerable drop in fatality to the introduction of a more intensive serotherapy. Moreover, since then, neither larger doses of serum, nor more active sulphonamides, nor the flavines, nor penicillin itself has in any way reduced this final hard core of cases sure to die.

The real questions at issue therefore seem to me to be:

(1) Is there more than one form of toxæmia in gas gangrene? One—the usual form, rarely seen now, directly related to the bacterial toxins; the other, forming most of our irreducible 30%, produced by other factors, possibly derived from tissues.

(2) That being decided—why does death occur and how can we prevent it?

To neither of these questions are we at present in a position to give an answer.

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Dr. Marjorie Macfarlane: The existence of a bacterial toxæmia in clinical gas gangrene has been doubted because of the failure to detect the toxin in blood samples from the patient. Evidence that the toxin is absorbed from the local lesion has, however, been furnished by the beneficial effect of antitoxin on the recovery rate from gas gangrene in the late war. An analysis of cases reported on Army Form I.1241 (Macfarlane, 1943) showed that in the group of patients who underwent amputation within six hours of diagnosis of the disease, the death-rate was significantly and substantially lower amongst those who also received antitoxin within this time, compared with those who received no antitoxin or only received it at a late stage of the disease. Since this antitoxin was usually given at the time of amputation, i.e. when the affected tissue and the source of the toxin had been eradicated, its beneficial effect is only explicable on the basis that it neutralized the specific toxin which had been acting after absorption as a systemic poison.

The statistical data obtained established in principle that the use of antitoxin gives a patient a better chance of recovery, but in the field antitoxin appears to be almost as essential as surgery for a good recovery rate. In the various campaigns of the British Army the recovery rate from gas gangrene ran parallel to the proportion of the cases receiving early and adequate treatment with antitoxin in addition to surgical treatment (MacLennan and Macfarlane, 1944). The rise in the mean recovery rate for all cases, from 30% in Sicily to 70 to 75% in the later stages of the Italian campaign and in the B.L.A., was substantially due to the wider and intensive use of antitoxin, and not simply to a general improvement in the conditions, or any attenuation of the disease; for the recovery rate amongst those receiving adequate antitoxin therapy showed a relatively slight improvement (from 65 to 75%) over the same period, in spite of better military conditions, experienced surgeons and the introduction of penicillin. The fact that with the best treatment possible the death-rate remained about 25% indicates, however, the existence of another cause of toxæmia in addition to the bacterial toxin (Macfarlane, 1945).

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control of the disease, had not been taken into account and provided for. As custodians of the international standard preparations we regarded this as a serious criticism because, if these antibodies were important in the control of the disease, they should be provided in the antiserum in adequate amounts and measured by reference to a more complete standard, or to a series of standards which, it was claimed, should be provided. Accordingly, following an important conference at Cambridge on April 5, 1941, at which this question was discussed, investigations have been carried out at Hampstead with the object of determining the relative importance of the various antigens on the causation, and of the antibodies to these occurring in *Cl. welchii* Type A antiserum in the prevention and treatment, of gas gangrene. Thanks to the co-operation of our friends at the Wellcome Physiological Research Laboratories at Beckenham, who have generously supplied us with the necessary specific antibody preparations, it has been possible to study the effect of these separate antibodies on the prevention of gas gangrene, and on the course of the disease, in experimentally infected guinea-pigs.

Evans (1943a) showed that a small dose of α antitoxin (free from θ antihæmolysin) given four hours before a dose of *Cl. welchii* A which produced θ hæmolysin and which proved fatal to unprotected guinea-pigs, afforded complete protection; the largest dose of θ anti-hæmolysin which could be administered, however, gave no protection whatever. Later in the same year (1943b) Evans showed that complete protection was afforded by a small dose of α antitoxin (free from antihyaluronidase) against a fatal infection produced by strains of *Cl. welchii* A which produced hyaluronidase: while antiserum containing antihyaluronidase (but free from α antitoxin) afforded no protection and failed to affect the course of the disease in guinea-pigs. Later, antisera containing larger quantities of θ antihæmolysin and antihyaluronidase respectively became available and it was shown that larger doses of these antibodies neither protected against the disease nor enhanced the protective value of α antitoxin. In a study of 30 strains of *Cl. welchii* A, Evans (1945a) showed that there was a close correlation between the power to produce α toxin in culture and virulence, while no such correlation could be demonstrated for hæmolysin or for hyaluronidase; further, he showed that complete protection against infection against 28 of these strains was afforded by a small dose (25 units) of α antitoxin. One strain, however, required 100, and another 200, units of α antitoxin for protection. The importance of α antitoxin is clearly brought out in these experiments and the results are of special interest in relation to the findings of Weinberg and Guillaumie (1938). Evans (1945b) has also shown that small doses of α antitoxin, free from anti-collagenase, afforded complete protection to guinea-pigs infected with strains of *Cl. welchii* A, which produced collagenase, while preparations of antiserum containing anticollagenase (and no α antitoxin) neither protected guinea-pigs nor enhanced the protective value of α antitoxin itself. In another series of experiments (1945c) Evans has shown that specific antitoxin administered intravenously after infection with *Cl. welchii* A, *Cl. œdematians* or *Cl. septicum* has a marked clinical effect on the course of the disease in guinea-pigs; and, although antitoxin could not influence the development of the lesions produced by the action of toxin on local tissue yet life was prolonged, especially if treatment had not been unduly delayed. Given early in the disease, the toxæmia was controlled, the power of the organism to proliferate was apparently restricted and the natural defence and recovery mechanisms of the guinea-pig came into operation; under certain conditions of experiment the animals recovered completely. In another experiment in which infection, ending fatally in untreated guinea-pigs, was established with a strain which produced collagenase, Evans (1945b) showed that small doses of α antitoxin (free from anti-collagenase) given four hours after infection had a marked effect on the course of the disease; and it was also shown that no significant difference in results was obtained whether the antitoxin was given intravenously or directly into the infected muscle. One other experiment was described which illustrated the importance of early surgery in the treatment of gas gangrene infections. Two exactly similar groups of guinea-pigs, 18 in each group, were injected with a virulent strain of *Cl. welchii* A. One group received no treatment whatever and all the 18 animals died within three days; four hours after infection an incision was made into the infected thigh muscle of each of the 18 animals of the second group, and in this case 13 animals survived for more than fourteen days and, of the 5 which died, life was prolonged to four and five days in three of these.

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Clinical Section

President—A. DICKSON WRIGHT, M.S., F.R.C.S.

[November 9, 1945]

Thiouracil Agranulocytosis: Recovery on Pyridoxine.—HERMON TAYLOR, M.D., M.Ch., F.R.C.S. Demonstrated by C. H. de Boer, M.B., B.Chir.

24.8.45: Mrs. J. D., aged 49, attended London Hospital with a moderate degree of thyrotoxicosis; ambulatory treatment with thiouracil, 100 mg. b.d. Toxic symptoms disappeared during ensuing six weeks; W.B.C. remained between 5,000 to 7,000; polymorphs 60%. Dosage reduced to 75 mg. thiouracil b.d. for next three weeks.

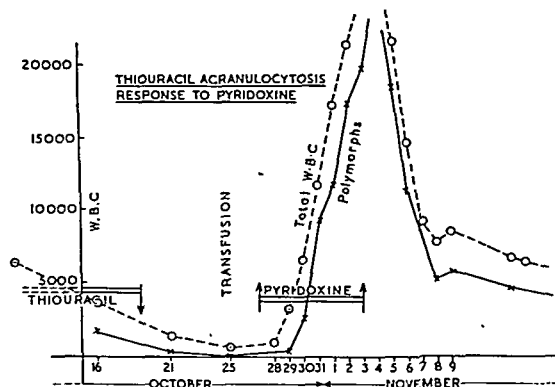
16.10.45: First abnormal count. W.B.C. 3,500; 50% polymorphs.

19.10.45: Thiouracil discontinued (total dose to date 10 grammes).

21.10.45: Patient felt ill, sore throat. W.B.C. 1,400; 4% polymorphs.

24.10.45: Admitted to hospital T. 102-6, P. 96. Flushed, ill, inflamed fauces.

25.10.45: Condition worse; fauces and pharynx covered with white patches (treated by gentian violet). W.B.C. 600; 3% polymorphs (18 polymorphs per c.mm.). Sternal marrow smear showed complete absence of all granulocytes. Blood transfusion given.



27.10.45: Jaundiced. Patient almost comatose, could be roused with difficulty. Passed no urine in twenty-four hours. Pyridoxine (vitamin B₆) therapy commenced on the advice of Professor Marrack; 150 mg. per day given intravenously.

28.10.45: W.B.C. 1,000.

29.10.45: Patient improved; less apathetic; throat less sore; could swallow soft solids for the first time. W.B.C. 3,000; 22% polymorphs.

30.10.45: Better. W.B.C. 6,600; 38% polymorphs.

31.10.45: Much better. W.B.C. 13,300; 71% polymorphs.

1.11.45: Sternal marrow smear now showed regeneration of granulocytes (*see Table*).

3.11.45: Patient convalescent. W.B.C. 23,800; 83% polymorphs. Red cell and platelet counts had remained materially unchanged throughout.

control of the disease, had not been taken into account and provided for. As custodians of the international standard preparations we regarded this as a serious criticism because, if these antibodies were important in the control of the disease, they should be provided in the antiserum in adequate amounts and measured by reference to a more complete standard, or to a series of standards which, it was claimed, should be provided. Accordingly, following an important conference at Cambridge on April 5, 1941, at which this question was discussed, investigations have been carried out at Hampstead with the object of determining the relative importance of the various antigens on the causation, and of the antibodies to these occurring in *Cl. welchii* Type A antiserum in the prevention and treatment, of gas gangrene. Thanks to the co-operation of our friends at the Wellcome Physiological Research Laboratories at Beckenham, who have generously supplied us with the necessary specific antibody preparations, it has been possible to study the effect of these separate antibodies on the prevention of gas gangrene, and on the course of the disease, in experimentally infected guinea-pigs.

Evans (1943a) showed that a small dose of a antitoxin (free from θ antihæmolyisin) given four hours before a dose of *Cl. welchii* A which produced θ hæmolyisin and which proved fatal to unprotected guinea-pigs, afforded complete protection; the largest dose of θ anti-hæmolyisin which could be administered, however, gave no protection whatever. Later in the same year (1943b) Evans showed that complete protection was afforded by a small dose of a antitoxin (free from antihyaluronidase) against a fatal infection produced by strains of *Cl. welchii* A which produced hyaluronidase; while antiserum containing antihyaluronidase (but free from a antitoxin) afforded no protection and failed to affect the course of the disease in guinea-pigs. Later, antisera containing larger quantities of θ antihæmolyisin and antihyaluronidase respectively became available and it was shown that larger doses of these antibodies neither protected against the disease nor enhanced the protective value of a antitoxin. In a study of 30 strains of *Cl. welchii* A, Evans (1945a) showed that there was a close correlation between the power to produce a toxin in culture and virulence, while no such correlation could be demonstrated for hæmolyisin or for hyaluronidase; further, he showed that complete protection against infection against 28 of these strains was afforded by a small dose (25 units) of a antitoxin. One strain, however, required 100, and another 200, units of a antitoxin for protection. The importance of a antitoxin is clearly brought out in these experiments and the results are of special interest in relation to the findings of Weinberg and Guillaumie (1938). Evans (1945b) has also shown that small doses of a antitoxin, free from anti-collagenase, afforded complete protection to guinea-pigs infected with strains of *Cl. welchii* A, which produced collagenase, while preparations of antiserum containing anticollagenase (and no a antitoxin) neither protected guinea-pigs nor enhanced the protective value of a antitoxin itself. In another series of experiments (1945c) Evans has shown that specific antitoxin administered intravenously after infection with *Cl. welchii* A, *Cl. œdematiens* or *Cl. septicum* has a marked clinical effect on the course of the disease in guinea-pigs; and, although antitoxin could not influence the development of the lesions produced by the action of toxin on local tissue yet life was prolonged, especially if treatment had not been unduly delayed. Given early in the disease, the toxæmia was controlled, the power of the organism to proliferate was apparently restricted and the natural defence and recovery mechanisms of the guinea-pig came into operation; under certain conditions of experiment the animals recovered completely. In another experiment in which infection, ending fatally in untreated guinea-pigs, was established with a strain which produced collagenase, Evans (1945b) showed that small doses of a antitoxin (free from anti-collagenase) given four hours after infection had a marked effect on the course of the disease; and it was also shown that no significant difference in results was obtained whether the antitoxin was given intravenously or directly into the infected muscle. One other experiment was described which illustrated the importance of early surgery in the treatment of gas gangrene infections. Two exactly similar groups of guinea-pigs, 18 in each group, were injected with a virulent strain of *Cl. welchii* A. One group received no treatment whatever and all the 18 animals died within three days; four hours after infection an incision was made into the infected thigh muscle of each of the 18 animals of the second group, and in this case 13 animals survived for more than fourteen days and, of the 5 which died, life was prolonged to four and five days in three of these.

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right hypochondrium. He had been constipated for a few days previously. The pain was continuous with no relief, causing nausea and repeated vomiting. He was admitted to hospital and later transferred to the London Hospital.

May 3, 1945 on admission, he was pale, ill-looking and in pain, occasionally retching with small vomits of bile-stained fluid. Jaundiced sclerotics. Tongue was furred. Slight general wasting and dehydration. Temperature 100°; pulse 100; respiration 24.

Abnormal physical signs.—Respiratory system: Lower right ribs prominent. Movement—right greater than left in lower part. P.N. dull at right base. Breath sounds; occasional rhonchi at right base. Liver enlarged upwards.

Abdomen: Liver tender and enlarged 2 fingerbreadths. Small "stab wound" scar in mid-epigastric region (site of abscess drainage).

C.V.S. and C.N.S. apparently normal.

Diagnosis.—Amœbic hepatitis with recurrent abscess.

Investigations.—Blood: Granulocytosis (leucocytes 21,200, polys. 92%), Hb. 102%. Stools: No amœbæ or cysts seen. No R.B.C. Van den Bergh reaction: Qualitative—biphasic reaction. Quantitative—4 mg. of bilirubin per 100 c.c. Alkaline phosphatase 12 units (normal 6 to 10 units). X-ray of chest: Slight increase of lung markings in right mid-zone. Right side of diaphragm raised and liver margin depressed.

Treatment and progress.—He was put on a high protein, low fat, low residue diet with extra glucose and fluids. Kapilon 20 mg. daily, Ascorbic acid 25 mg. b.d. and a course of emetine hydrochloride 1 grain daily started. There was no response to this. Attempted aspirations produced pure blood only—culture sterile. His general condition remained about the same.

He was seen by Sir Philip Manson-Bahr who reported:

"There is no doubt about the diagnosis in this case. There is a large liver abscess subdiaphragmatic in the posterior part of the right lobe of the liver. It ascends to the 7th rib on the scapular line.

"There is a marked pleuritic rub which indicates that the abscess is about to rupture into the pleura at the angle of the right scapula. I suggest that this is primarily an amœbic abscess which has recurred after two years and that the pus is now secondarily infected with some micro-organism.—? *B. coli* or *B. endometritidis*."

On his advice rib resection and exploration of the liver were carried out through a transpleural approach. A small amount of thick pus was encountered. Further exploration to isolate cavity was unsuccessful; assumed to be many small cavities.

Subsequent chest X-ray showed hydropneumothorax.

Culture from aspirated fluid—profuse growth of *Staphylococcus pyogenes*, sensitive to penicillin.

A five-day course of penicillin (total 553,000 units) resulted in slight improvement. Jaundice was less. Pyrexia continued with occasional rigors.

Further swab showed growth of aerobic and anaerobic *B. coli*, sensitive to sulphathiazole.

A combined course of sulphamezathine 30 grammes and penicillin 720,000 units was given followed by a twelve-day course of emetine bismuth iodide 1 grain t.d.s., then carbazone 0.25 mg. b.d. for ten days.

Subsequent progress was satisfactory. He remained afebrile. Normal pulse. No rigors. Gained weight. No amœbæ or cysts seen in three stool reports.

Drainage-wound healed well. X-ray of chest showed complete re-expansion of lung; no pleural effusion.

[December 14, 1945]

Primary Splenic Granulocytopenia and Lymphopenia.—HERBERT LEVY, M.D., M.R.C.P.

Emily O., aged 69. Admitted to hospital May 1945 for conjunctivitis. Deformity of fingers since about age of 56; has been living in L.C.C. Institutions ever since. Typhoid fever about twenty years ago.

On examination.—Rather frail; somewhat poor mental power; not looking ill. Iritis and conjunctivitis; corneal nebulae. Spleen 5 in. below costal margin, reaching nearly mid-line and lower pole about midway between levels of umbilicus and symphysis pubis. Small axillary and inguinal lymph nodes. Liver 1½ in. below costal margin. Moderate degree of lower dorsal kyphosis. Arteriosclerosis of peripheral vessels. Calcified uterine fibroid. Skiagram of chest: increased striation of all lung fields; right diaphragm higher than left.

Flexion deformity of both little fingers in proximal interphalangeal joint; hyperextension of distal interphalangeal joints. Undue mobility of interphalangeal joint of thumbs; in

Bone-marrow smears	25.10.45 Before pyridoxine	1.11.45 After 5 days pyridoxine
	%	%
Polymorph series.—Neutrophils	—	24
Eosinos.	—	—
Transitionals	—	18
Neutromyelocytes	—	28
Promyelocytes	26	7.5
Myeloblasts	4	1
Other cells.—Lymphocytes	49	8
Plasma cells	1	—
Monocytes	—	—
Early erythroblasts	4	3.5
Late erythroblasts	5	2.5
Normoblasts	11	7.5

Comment.—The use of pyridoxine in the treatment of agranulocytosis was first suggested by Cantor and Scott in 1944 following a report of the occurrence of a leucocytosis in cases of anaemia treated with vitamin B₆.

Previous to 1931 the treatment of this condition was by: elimination of the cause, if known, and repeated blood transfusions whose value is doubted. In 1931 pentnucleotide was introduced to stimulate the release of the myeloid cells. Jackson and Tighe (1939) reported a reduction of the mortality to 30% from its use; Fettes and Whitby (1935) had less success. Jackson showed that it had little effect where there is aplasia of the marrow. In 1938 some help was gained from the use of bone-marrow concentrates for agranulocytosis when pentnucleotide had failed, but this has not been fully confirmed. Fatal toxic reactions to thiouracil are not common, 1% of 600 published cases. When agranulocytosis occurs, however, it is associated with marrow atrophy and is rapidly fatal in spite of transfusion and pentnucleotide. It is suggested that pyridoxine intravenously may restore the marrow function even at a late stage in the disease.

POSTSCRIPT (19.11.45).—The patient was given another course of pyridoxine, 50 mg. per day for four days, intravenously. This had no effect whatsoever on her total white or differential count.

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Hepatitis with Abscess Secondarily Infected by *Staphylococcus pyogenes* and *B. coli*.— R. G. BIRD, M.B.

This soldier, W. W., aged 37, was transferred to the London Hospital on 3.5.45 complaining of sharp pains in the right upper abdomen.

History.—Passed A 1 into the Army on September 12, 1940, having had no previous serious illness. He remained well until June 1941 when, during the first two weeks of being in Africa, he had attacks of nausea and diarrhoea with frequent fluid stools—no blood, no mucus. Without treatment he became symptom-free, remaining so (except for a mild attack of bronchopneumonia in January 1943) until October 1943 when a very bad attack of symptoms as in June 1941 occurred and he was admitted to hospital in Cairo. Amoebic dysentery was diagnosed. A full course of emetine treatment was given, during which a lump appeared in the right epigastric area. He was told it was an amoebic abscess. It was aspirated thirteen times. He remained in this hospital five months.

By February 1944 he appeared well again and was repatriated. Given convalescent leave, then in April discharged from hospital, category C 2, recommended for light duties for six months.

Apart from occasional vague epigastric discomfort at night, he remained symptom-free until April 1945 when, while on leave, he was suddenly seized by sharp, gnawing pain in

Blood-counts.—

1945	July 9	July 17	July 31	Aug. 3	Sept. 20	Dec. 12
R.B.C. (millions)	4.7	4.58	3.86	4.28		4.45
Hb. (Haldane)	64	74	74	76	90	88
W.B.C. ...	29,200	34,800	28,400	28,400	20,750	13,000
Poly. Neutros.	11,096	13,572	13,064	16,472	7,678	7,540
Eosinos.	292	2,088	568	1,420	1,452	910
Basos. ...	—	—	—	—	207	260
Lymphos. ...	17,228	18,444	13,916	9,656	11,206	3,250
Monos. ...	584	696	852	852	207	1,040

Most of the lymphocytes have either an immature (abnormally basophil) cytoplasm or a nucleus of the Rieder cell type or an immature nucleus, many cells having also an abnormally large amount of, often coarse, azure granules.

Sternal marrow count: Cells of myeloid series 54.46% out of which 14.84% eosinophils; 1% lymphoblasts; 30% lymphocytes; 2.5% plasma cells; 11.83% nucleated R.B.C.; 0.16% Ferrata cells. Out of 600 cells only two, both erythroblasts, were in mitosis. A few of the band-shaped neutrophils were abnormally large. Lymphocytes in bone-marrow had same appearances as those in peripheral blood.

August 1945: Serum—cholesterol 184 mg.%, protein 7.8 grammes%, albumin 4.1 grammes%, globulin 3.7 grammes%, uric acid 3.3 mg.%. .

December 1945: Glucose tolerance test (50 grammes orally):

Fasting blood sugar	100 mg.%
30 min. after glucose administration	218
60 " " "	"	"	159, no glycosuria
90 " " "	"	"	123
120 " " "	"	"	104, no glycosuria
150 " " "	"	"	70

Biopsy of skin: "Strongly in favour of a (malignant) reticulosis; the sections are not consistent with a dermatitis, eczema, or psoriasis, conditions clinically indistinguishable from that of your patient" (W. Freudenthal).

Biopsy of inguinal lymph node: "Largely a reactive change of the lipomelanotic reticulosis type, but there are in the medulla clumps of atypical lymphoid cells whose nature it is difficult to determine and the same is true with regard to the foci of the lymphoid proliferation in the superficial dermis; in this case the skin changes are more marked than I have seen before and so there is a possibility that it is associated with a primary blood disease but I am a bit sceptical about it and believe that it does correspond to this group [lipomelanotic reticulosis] of conditions" (A. H. T. Robb-Smith).

General condition now rather better than in summer months. Exfoliation recently much diminished; skin red to dusky red, rather purple over lower back; texture as before ("elephant skin"). Afebrile and not confined to bed.

For permission to demonstrate the patient I wish to thank Dr. B. Young, Medical Superintendent, St. Alfege's (L.C.C.) Hospital, under whose care he now is. For the peripheral blood-counts and biochemical tests I am obliged to Drs. R. F. L. Hewlett and E. N. Allott.

Comment.—When first confronted with this case, the problem was: is the erythrodermia a manifestation of a lymphatic leukaemia or of a Hodgkin or are the lymph-node enlargements secondary to the skin affection? A certain bias in favour of lymphatic leukaemia began to wane after seeing the peripheral blood film. The sternal marrow picture made the possibility of a leukaemia still less likely; while about 25% lymphocytes are the upper normal limit, a finding of 30% does not yet allow the diagnosis of lymphatic leukaemia unless this is based on other evidence; and the rather high eosinophilia (subsequently also found in the peripheral blood) pointed towards reactive change or Hodgkin. The various abnormalities of the lymphocytes also favoured the probability of a lymphatic reaction rather than of a leukaemia. Hodgkin's disease could definitely be excluded by the lymph-node biopsy, and Dr. Robb-Smith's opinion regarding leukaemia is quoted above. On looking more closely through the literature of cases of this kind reported as lymphatic, or in the last two decades quite often as monocytic leukaemia, there seems little doubt that this diagnosis stands in at least a good number of cases on rather weak legs. In the

resting position the phalanges stand to each other in hyperextension. Ulnar deflection of second to little fingers of both hands. Halluces valgi. Some toes in hammertoe position. Skiagram of hands: bony ankylosis of proximal interphalangeal joints of both little fingers; spaces of other joints in normal limits and no periarticular atrophy or sclerosis of bone.

Blood-counts.—

1945	May 15	May 16	July 18	Aug. 24	Oct. 3	Nov. 9
R.B.C. (millions)	3.91	3.99	4.4	4.23	4.52	
Hb. (Haldane) ...	82	82	74	85	86	
W.B.C. ...	1,000	900	1,200	770	500	1,750
Polys.: Neutros.	200	216	492	123	85	613
Eosinos.	40	36	—	8	15	52
Basos. ...	20	—	—	—	—	—
Lymphos. ...	620	468	612	616	340	998
Monos. ...	120	180	96	23	60	87

Platelets normal in appearance; numbers low on one occasion but within normal limits on all other occasions.

16.5.45: M.C.V. 92 cu. μ . M.C.Hb. concentration 33%.

Sternal marrow: very active erythropoiesis and myelopoiesis; erythroblasts of normal, non-megaloblastic series. Megakaryocytes rather abundant. No other quantitative or qualitative abnormality noted.

Serum—protein 6.4 grammes%, albumin 3.7 grammes%, globulin 2.7 grammes%, bilirubin 0.2 mg.%, phosphatase (alkaline) 7.5 units. Takata-Ara and formol gel: both positive, moderately strong. Blood urea 38 mg.%. Serum cholesterol 178 mg.%.

Pyridoxine hydrochloride was given intravenously: 150 mg. on December 8 and 9, and 100 mg. on December 11, 12, and 13. Subsequent blood-counts:

1945	Dec. 10	Dec. 12	Dec. 14
W.B.C. ...	2,450	1,725	1,275
Polys.: Neutros. ...	490	259	128
Eosinos. ...	220	138	102
Basos. ...	25	17	—
Lymphos. ...	1,543	1,156	892
Monos. ...	172	155	153

No change in general condition since under observation. The increase in eosinophil polymorphs and lymphocytes at the time of the pyridoxine treatment was possibly related to a recent flare-up of the iritis.

For the peripheral blood-counts and biochemical tests I am obliged to Dr. J. M. Alston.

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Generalized Erythrodermia (? Malignant Reticulosis).—HERBERT LEVY, M.D., M.R.C.P.

William J., aged 70. Past and family history irrelevant. About 1939 red, itchy rash over middle of chest which was gradually spreading, losing at the same time its pruriginous character; surface of whole body involved by about 1944. Admitted to hospital May 1945 for carbuncle of neck. Irregular intermittent pyrexia up to 101° during May 1945; later on occasional bouts of fever subsiding in a few hours. July 1945 a few pyodermic lesions.

On examination (July 1945).—Generalized erythrodermia, with bran-like exfoliation especially on face and scalp and considerable thickening and stiffness of entire skin. Gross dystrophy of all nails; visibly enlarged inguinal lymph nodes, cervical and axillary lymph nodes up to cherry-stone or date-stone size. Tongue and visible mucous membranes normal in appearance except for marked injection of palpebral conjunctivae. Spleen not palpable; liver slightly enlarged.

He was discharged on July 18, 1945, with regular rhythm and normal rate and was put on a maintenance dose of quinidine sulph. 3 grains b.d. He felt well until September 1945 when tachycardia recurred and he was readmitted to Guy's Hospital on September 9, 1945; paroxysmal auricular tachycardia with 2:1 block again was found. Alternation in cycle length of the P-P intervals was marked (see fig. 1) (Barker, Johnston and Wilson, 1943). Tinct. digitalis m xv , q.i.d. given during two and a half days, abolished the attack and on September 28, 1945, a ventricular rate of 65 with regular rhythm was recorded. A maintenance dose of tinct. digitalis m vii once daily produced coupling owing to ventricular extrasystoles. With quinidine sulph. 3 grains six times a day, started on October 10, regular rhythm (rate 60-70) persisted until October 21 when both ventricular and pulse-rates rose to about 128. Electrocardiograms (October 22, 23 and 24) showed recurrence of paroxysmal auricular tachycardia; the ventricular rhythm being a little faster than *half* the auricular rate there was occasional interference with the ventricular rhythm by conducted auricular beats: dissociation with interference. Most of the features known to occur in the ordinary form of dissociation with interference (in which a faster atrioventricular rhythm and a slower sinus rhythm co-exist) (Schott, 1937) were observed in this case: The R-R intervals produced by conducted beats were shorter than the R-R intervals between two successive atrioventricular beats; the R-R interval following a conducted beat was shorter than the R-R intervals of successive atrioventricular beats if this beat too was produced by a (second) conducted beat (fig. 2) or was materially lengthened if an auricular impulse was conducted through the atrioventricular centre, there interfering with the production of the atrioventricular rhythm, but being blocked below the atrioventricular centre failed to yield a ventricular response (fig. 3). A peculiar feature of the arrhythmia on October 24 (see fig. 4) was that the onset of conducted beats was invariably preceded by an acceleration of both the auricular and atrioventricular rhythms, the P-P intervals being shortened from 27-28 to 24-25/100 seconds and the R-R intervals from 52-56 to 49-50/100 seconds. Simultaneous variations in the rate of two co-existing rhythms have been described by Scharf and Weiser (1924) and attributed to vagal influence. A diagram of a continuous record of 103 ventricular cycles, obtained on October 24, is shown in fig. 4.

Tinct. digitalis m vii , b.d. for two days and t.d.s. for another two days abolished the attack on November 1, sinus (? ectopic auricular) rhythm, regular, rate 71, ensuing. From November 3 onwards he was given tinct. digitalis m vii , b.d. and quinidine sulph. 5 grains t.d.s. on alternate days with clinical improvement and persistent regular rhythm of normal rate. Occasional coupled beats were heard on auscultation and recorded on December 4 whereupon the dose of digitalis was reduced to m v .

Repeated radiological examinations of the chest failed to show any enlargement of the left auricle, nor was a double contour on the right border found again. The right auricle was markedly enlarged. No mitral diastolic murmur was heard.

Grateful acknowledgment is made to Dr. A. H. Douthwaite, under whose care the patient was admitted to Guy's Hospital, for his kind permission to demonstrate the case again and publish his notes.

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Dr. A. Elkeles agrees that this is not a case of mitral stenosis. The enlargement of the right heart, which seems to be mainly caused by dilatation of the right auricle, is, however, difficult to explain. The radiograms of the chest taken in the posterior-anterior and particularly in the right oblique position with an opaque oesophagus demonstrate the enlargement of the right auricle by showing a definite bulge of the terminal part of the oesophagus, but no displacement of the lower third of the oesophagus is present, which excludes dilatation of the left auricle. Since isolated enlargement of the right auricle is so far unknown in organic heart disease it may be suggested that in this particular case of severe and long-continued paroxysmal auricular tachycardia with A-V block the auricles are subjected to the main strain, and incomplete emptying of the right auricle may give rise to increased intra-auricular pressure with consequent dilatation. Recent observations by Campbell, Currie, Hunter and Evans have shown that even after single attacks of paroxysmal auricular tachycardia without A-V block inversion of T waves were present in the E.C.G., which although of a temporary character may remain for some months. These authors explain the temporary inversion of T waves as a result of extra strain on the heart muscle during the attacks. It may be of interest to investigate whether isolated enlargement of the right auricle may be a feature in paroxysmal auricular tachycardia with A-V block.

valuable monograph on leukaemia by Forkner (1938) the conclusions of the various authors quoted by him seem unfortunately rather unhesitatingly accepted. An excellent account of the condition was given by Sequeira and Panton (1925) (quoted by Whittle and Hughes-Jones, 1943) who proposed the term lymphoblastic erythrodermia. In the older dermatological literature, Hebra's term of pityriasis rubra was probably used in too wide a sense, including also cases showing little, if any, pityriasis. In this condition, if I understand the term correctly, one finds thinning of the skin rather than stiffness connected with thickening. The term "lipo-melanin reticulosis", used in Dr. Robb-Smith's report, was coined by Pautrier and Woringer (1937) but they proposed it as a rather generic term describing the presence of melanin and some lipid substance in abnormally increased amounts in the lymph nodes in many forms of erythrodermia, including those secondary to eczema, psoriasis, pemphigus, arsenic poisoning, &c., and they thought that the accumulation of these substances in the lymph nodes is due to a disturbance of their exchange between skin and epidermis.

Regarding any form of systemic treatment, the literature is silent and in Fraser's case (1943) the eventual improvement was not attributed by the author to a previous course of X-ray treatment.

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Splenomegaly with Leucopenia.—A. L. WINGFIELD, M.D.

M. A., aged 28. Indian Scaman. Admitted 13.9.45 with sore throat, pain in the neck and pain in abdomen. Mild jaundice was present but soon disappeared.

On examination.—Looked ill. Temperature 100.4. P. 90. R. 20. Follicular tonsillitis on left side with enlarged and tender cervical glands. Heart and lungs normal. B.P. 100/60. Liver enlarged two fingers, spleen enlarged to level of umbilicus. Notch easily felt. Throat swab no K.L.B. Blood films for malaria negative.

6.10.45: Hb. 40%. W.B.C. 1,800 per c.mm. Van den Bergh—indirect positive. Fouchet's test—strong positive. Splenic and sternal punctures negative for Leishman-Donovan bodies and malaria parasites. Formol-gel and urea-stibamine tests negative.

Faeces: One *Ascaris lumbricoides* found, subsequently no ova or cysts. Temperature persisted at about 101° and in view of the granulocytopenia treatment was started with Pentide and Plexan. The temperature gradually settled and was normal from October 2 to 7.

R.B.C. 1,430,000 per c.mm. Hb. 35%. W.B.C. 3,300 per c.mm. Polymorphs 40%. No anisocytosis or poikilocytosis.

A spike of temperature on 7.10.45 led to antimalarial treatment and the temperature again settled and remained normal until 24.11.45.

Recent investigations.—Widal reaction negative for typhoid and *abortus* organisms. W.R. negative.

Blood-count (28.11.45).—R.B.C. 2,800,000 per c.mm.; Hb. 63%; W.B.C. 2,600 per c.mm. Differential white: Polys. 42%, small lymphos. 50%, large monos. 4%, large lymphos. 2%, eosinos. 2%. No malaria parasites seen.

In view of the recurrence of fever neostibosan is now being given. Splenic enlargement unchanged but recently abdominal distension. There is now very little fever.

Kala-azar is the obvious diagnosis but all tests for this are negative.

Dr. Herbert Levy said that had this syndrome been found in a European he would have first thought of Hodgkin's disease. Pernicious anaemia seemed another possibility; part of the splenic enlargement might in this case be due to previous malaria.

Paroxysmal Auricular Tachycardia with Auriculo-Ventricular Block; Follow Up; Transient Dissociation with Interference.—A. SCHOTT, M.D.

Male, aged 42. Previously demonstrated on February 9, 1945.

In October 1944 he caught a "heavy cold" and five days afterwards had a sudden attack of very marked shortness of breath with a choking sensation, substernal pain and tachycardia and collapsed. He was first admitted to Guy's Hospital on December 1, 1944, where a diagnosis of paroxysmal auricular tachycardia with auriculo-ventricular block was made. For further details see Schott, 1945.

He was discharged on July 18, 1945, with regular rhythm and normal rate and was put on a maintenance dose of quinidine sulph. 3 grains b.d. He felt well until September 1945 when tachycardia recurred and he was readmitted to Guy's Hospital on September 9, 1945; paroxysmal auricular tachycardia with 2:1 block again was found. Alternation in cycle length of the P-P intervals was marked (see fig. 1) (Barker, Johnston and Wilson, 1943). Tinct. digitalis m xv, q.i.d. given during two and a half days, abolished the attack and on September 28, 1945, a ventricular rate of 65 with regular rhythm was recorded. A maintenance dose of tinct. digitalis m vii once daily produced coupling owing to ventricular extrasystoles. With quinidine sulph. 3 grains six times a day, started on October 10, regular rhythm (rate 60-70) persisted until October 21 when both ventricular and pulse-rates rose to about 128. Electrocardiograms (October 22, 23 and 24) showed recurrence of paroxysmal auricular tachycardia; the ventricular rhythm being a little faster than *half* the auricular rate there was occasional interference with the ventricular rhythm by conducted auricular beats; dissociation with interference. Most of the features known to occur in the ordinary form of dissociation with interference (in which a faster atrioventricular rhythm and a slower sinus rhythm co-exist) (Schott, 1937) were observed in this case: The R-R intervals produced by conducted beats were shorter than the R-R intervals between two successive atrioventricular beats; the R-R interval following a conducted beat was shorter than the R-R intervals of successive atrioventricular beats if this beat too was produced by a (second) conducted beat (fig. 2) or was materially lengthened if an auricular impulse was conducted through the atrioventricular centre, there interfering with the production of the atrioventricular rhythm, but being blocked below the atrioventricular centre failed to yield a ventricular response (fig. 3). A peculiar feature of the arrhythmia on October 24 (see fig. 4) was that the onset of conducted beats was invariably preceded by an acceleration of both the auricular and atrioventricular rhythms, the P-P intervals being shortened from 27-28 to 24-25/100 seconds and the R-R intervals from 52-56 to 49-50/100 seconds. Simultaneous variations in the rate of two co-existing rhythms have been described by Scharf and Weiser (1924) and attributed to vagal influence. A diagram of a continuous record of 103 ventricular cycles, obtained on October 24, is shown in fig. 4.

Tinct. digitalis m vii, b.d. for two days and t.d.s. for another two days abolished the attack on November 1, sinus (? ectopic auricular) rhythm, regular, rate 71, ensuing. From November 3 onwards he was given tinct. digitalis m vii, b.d. and quinidine sulph. 5 grains t.d.s. on alternate days with clinical improvement and persistent regular rhythm of normal rate. Occasional coupled beats were heard on auscultation and recorded on December 4 whereupon the dose of digitalis was reduced to m v.

Repeated radiological examinations of the chest failed to show any enlargement of the left auricle, nor was a double contour on the right border found again. The right auricle was markedly enlarged. No mitral diastolic murmur was heard.

Grateful acknowledgment is made to Dr. A. H. Douthwaite, under whose care the patient was admitted to Guy's Hospital, for his kind permission to demonstrate the case again and publish his notes.

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Dr. A. Elkeles agrees that this is not a case of mitral stenosis. The enlargement of the right heart, which seems to be mainly caused by dilatation of the right auricle, is, however, difficult to explain. The radiograms of the chest taken in the posterior-anterior and particularly in the right oblique position with an opaque œsophagus demonstrate the enlargement of the right auricle by showing a definite bulge of the terminal part of the œsophagus, but no displacement of the lower third of the œsophagus is present, which excludes dilatation of the left auricle. Since isolated enlargement of the right auricle is so far unknown in organic heart disease it may be suggested that in this particular case of severe and long-continued paroxysmal auricular tachycardia with A-V block the auricles are subjected to the main strain, and incomplete emptying of the right auricle may give rise to increased intra-auricular pressure with consequent dilatation. Recent observations by Campbell, Currie, Hunter and Evans have shown that even after single attacks of paroxysmal auricular tachycardia without A-V block inversion of T waves were present in the E.C.G., which although of a temporary character may remain for some months. These authors explain the temporary inversion of T waves as a result of extra strain on the heart muscle during the attacks. It may be of interest to investigate whether isolated enlargement of the right auricle may be a feature in paroxysmal auricular tachycardia with A-V block.

Para-oesophageal Hernia as a Cause of Recurrent Gastro-intestinal Hæmorrhage.—

A. ELKELES, M.D.

Mrs. R. L., aged 75. February 1943: Complained of general weakness, restlessness and empty feeling in the head. A few days previous to examination urgent and frequent desire to open bowels was felt and tarry stools were observed. These symptoms have recurred in varying intervals for the last twenty-five years (approximately once or twice yearly). During these attacks patient is confined to bed for a week or two.

On examination.—Patient very pale but well nourished. Lungs, heart and blood-pressure normal. Abdomen: No palpable tumour. Blood: Marked secondary anaemia. Urine: Albumin, sugar negative. Faeces: occult blood strongly positive.

Radiological examination: Round translucent shadow, the size of a large orange behind the heart (fig. 1). Barium meal revealed this shadow to be caused by protrusion of the proximal part of the stomach into the posterior left mediastinum. Œsophagus shows a diverticulum in its middle third (fig. 2). In the Trendelenburg position (right oblique) the lower third of the Œsophagus is elevated above the diaphragm and lies beside the herniated part of the stomach. The Œsophagus is of normal length (fig. 3). No evidence of peptic pathology or neoplasm in the gastro-intestinal tract, no polyposis of large intestine detected.

Course.—Satisfactory recovery and restoration of blood picture to normal on iron medication.

Re-examination (November 1945).—X-ray findings of Œsophagus and stomach unchanged. Only one attack of melæna since February 1943. Now symptom-free.

Comment.—Recently another case of para-oesophageal hernia in a male aged 70 was observed by me. Severe secondary anaemia was the only clinical sign. Diet and iron medication brought about a quick recovery. These cases and evidence from the literature indicate that gastro-intestinal hæmorrhage or severe anaemia may sometimes be the only clinical signs in para-oesophageal hernia. This condition should therefore be included in the differential diagnosis of pathological processes responsible for gastro-intestinal bleeding in advancing years. Hæmorrhage in these cases may be caused by congestion of the mucosa, by small erosions or even ulceration of the protruded stomach, changes which can be visualized by gastroscopic examination. Surgical intervention in para-oesophageal hernia, even when associated with gastro-intestinal bleeding, is not always necessary, and should only be resorted to if incarceration of the stomach in the Œsophageal hiatus with symptoms of obstruction occur or when medical treatment fails to control recurrent hæmorrhages.



FIG. 1.—Postero-anterior position: proximal half of stomach lies behind the heart.



FIG. 2.—Right oblique position: diverticulum of middle third of œsophagus is seen above the apex of the protruded stomach.



FIG. 3.—Trendelenburg position—right oblique; the parallel mucosal folds of the œsophagus can be seen through the gas-bubble of the protruded part of the stomach.

presenting this syndrome. There are records in the literature of 4 more cases, one recorded by Loeper, Lemaine and Patel—they suggested that the Chauffard-Still syndrome might be looked upon as one of the reticulo-endothelioses with the spleen as the essential site of the disease.

The rationale of this treatment is not known, but the clinical results have been encouraging and some patients have now been followed up for seven years.

In my opinion rheumatoid arthritis is a psychosomatic syndrome in which metabolic and psychological factors appear to play a more important role than does focal infection. There are certain points of interest which may give a possible clue as to the reason for the clinical improvement: In (1) starvation, (2) pregnancy (4th to 8th month), (3) jaundice (incidental, infective, or obstructive), it is the experience of clinicians that there is often a dramatic diminution in the severity of the symptoms of rheumatoid arthritis. This improvement, however, is of short duration. In all these conditions there is a retention of cholesterol in the blood. After splenectomy for acholuric jaundice the blood cholesterol is said to rise. Cholesterol is said by Herman Zondek to be the mother-substance of hormones, vitamins and carcinogenous substances. From the oxidation of certain side-chains of the cholesterol formula are derived: (a) the nucleus of bile salts, (b) testosterone, (c) steroids of the adrenal cortex, (d) stilboestrol: all substances which are used by clinicians in the treatment of rheumatoid arthritis.

[February 8, 1946]

Chronic Haemolytic Polycythæmia.—LEO RAU, M.D., M.R.C.P., R. J. V. PULVERTAFT, M.D., F.R.C.P., and J. G. HUMBLE, M.R.C.S., L.R.C.P.

Mrs. D., aged 37, was first seen by one of us (L. R.) in November 1945 complaining of general fatigue, dyspnœa, ulcers of her legs and peculiar blue spots on her nose, cheeks and both legs.

Good health until 1940 but in that year noticed the development of brown spots on her right leg. These spots developed into an ulcer. In 1943 she again started an ulcer of the right leg. Then she noticed some discoloration of her face, ever since she had the symptoms described above.

She has one boy aged 9; at the time of the pregnancy there were no complications, but she had a severe post-partum hæmorrhage. Further, she had severe hæmorrhage after the extraction of some teeth.

Family history.—Her mother has suffered from pernicious anæmia since 1942, and her blood-count is now normal. Mrs. D. is one of nine children, one of her sisters had a hysterectomy for fibroids and another, who is now 29, had a goitre removed.

On examination.—Well covered, very marked cyanosis of nose, chin and cheeks. No jaundice, or œdema. No glands palpable, but the spleen is enormously enlarged, filling almost two-thirds of the abdomen. The liver is easily palpable. The fundi are normal. In November 1945 there were several small ulcers of the lower thirds of both legs. Still more striking were venectasie of the stellate type with centripetal flow. B.P. 135/85. P. 66-72.

Investigations.—Blood-count: R.B.C. 6,530,000 per c.mm.; Hb. 140%; W.B.C. 9,200 per c.mm. Polys. 60%, lymphos. 30%, monos. 4%, eosinos. 4% and basos. 2%. One normoblast was found and there was marked poikilocytosis, anisocytosis and spherocytosis. Platelet count of 95,000 per c.mm. Serum bilirubin 1.6 mg.%. (Indirect.)

X-ray of skull and gall-bladder normal. X-ray of abdomen showed an enormous spleen.

The diagnosis of chronic hæmolytic polycythæmia was made.

Further investigations.—Reticulocyte count 3%. Fragility of R.B.C.'s from 0.3% to 0.55% NaCl.

Lastly her father, mother, two sisters and three brothers were examined, and all the blood films and reticulocyte counts were normal.

Comment.—The outstanding features of her case are polycythæmia, splenomegaly, and ulcers and venectasie of the legs. Clinically ulcers of the legs as in Mrs. D. occur only in acholuric jaundice and in sickle-celled anæmia. The investigations carried out in this case clearly demonstrate the presence of all the characteristics of acholuric jaundice. Usually patients with this disease have hæmolytic anæmia, but Mrs. D. produced polycythæmia as a sign of hypercompensation of her bone-marrow.

Splenectomy in the Treatment of the Rheumatoid Type of Arthritis.—FRANCIS BACH, D.M.

J. G., an unmarried girl aged 22, a clerk, was admitted under my care to the Rheumatic Unit at St. Stephen's Hospital on 10.7.45, suffering from the rheumatoid type of arthritis in an advanced and active phase.

Past history.—She is a shy, retiring girl, the youngest child of elderly parents. Three years ago she was seen by me at Out-patients, with a swelling of one finger. Diagnosis of rheumatoid arthritis was made. Treatment was instituted, but within a year she had marked swelling of the elbows, wrists, hands, knees, and ankles. Her condition progressed and she was admitted to hospital. Prior to admission she had lost weight, she felt ill, and had no appetite.

She was a tense, worried, underweight girl, with marked poor posture, marked deformity of the hands with wasting of the interossei muscles, slight ulnar deviation, limitation of dorsiflexion of the wrists, muscle spasm and limitation of elbow extension, slight limitation of hip movement, effusion in both knees with limitation of knee flexion, swelling of the ankles with limitation of dorsiflexion, deformity of the toes, limitation of shoulder movement. Epitrochlear, cervical, and inguinal glands were enlarged. The spleen was not palpable. There was a post-pharyngeal hyperplasia.

Family history.—Mother diabetic, nothing else of immediate interest.

Special investigations on admission.—Temperature normal, blood sedimentation 40 mm. Westergren at end of first hour. Blood-count: R.B.C. 5,000,000; Hb. 106%; W.B.C. 7,300. Polys. 67%, lymphos. 22%, monos. 9%, eosinos. 2%, basos. 0. Urine analysis normal. Throat swab no K.L.B. or hæmolytic strept. X-ray slight opacity of the antrum. Hands early rheumatoid type of change with diminution of joint space in proximal interpharyngeal joints; chest catarrhal signs. Wassermann and Kahn negative; blood urea 35 mg. per 100 ml., uric acid 2.7 mg. per 100 ml., van den Bergh direct action negative, indirect action less than 0.5 units bilirubin. Takata-Ara reaction suspicious. Thymol turbidity tests 5 units. Blood-sugar curve: Before sugar 70, subsequently 83, 88, 100, 76 mg. for 100 ml. Urine no sugar. Fæces: undigested muscle fibres, no starch detected. Total fat 23.8% of dried fæces, neutral fat 6.3%, free fatty acid 3.7%, combined fatty acid 13.8%, split fat 17.5%, unsplit fat 6.3%. Blood platelets 180,000 per c.mm., bleeding time normal. C.D.T. anti-complementary.

Psychological report: Highly strung nervous type. Reactions are purely those of the anxiety type with a good appreciation of her own difficulties. No evidence of any tendency to seek escape in somatic disability, and no evidence of hysterical temperament. I do not feel that there is a psychogenic factor in her condition (Dr. Dalziel).

Treatment included rest, full diet, extra vitamins, amytal $\frac{3}{4}$ grain q.i.d., prostigmine 15 mg. t.d.s. for one week, insulin 10 units t.d.s., a.c.; physiotherapy in the form of relaxation exercises; splints to hands, knees, and feet; heat and painless movements, breathing and postural exercises on slings, short wave galvanism, faradism to quadriceps muscles, &c. She failed to improve.

At my suggestion Mr. Waters performed splenectomy on her on 6.11.45. There was immediate improvement in her general health, with marked reduction of muscle spasm and joint swelling. The post-operative period was uneventful. She continued with her physical treatment, and within a fortnight was able to walk about the ward with little discomfort or disability. She is now back at work as a clerk.

Immediately before operation the blood platelet count was 392,000. After operation this increased to 480,000. The blood cholesterol was 160 mg. per 100 ml.

This patient is shown to demonstrate the possible value of splenectomy in the treatment of rheumatoid arthritis. She is one of a series of 8 patients under my care who have been carefully selected, and have failed to respond to the known, recognized methods of treatment.

The purpose of the operation is to reduce pain and muscle spasm, and, when present, pyrexia, and to try to prevent the further progress of crippling.

In 1940 with Oswald Savage I published in the *Annals of the Rheumatic Diseases* the detailed reports of three of my patients on whom splenectomy had been performed. Since then in 5 more patients this operation has been performed at my instigation.

In 1930 Paul Chevallier emphasized the similarity of the Chauffard-Still syndrome to the arthritic manifestations of Hanot's "biliary cirrhosis", described the ineffectiveness of the various kinds of treatment, and noted that in no instance had the spleen been removed. In 1932 Hanrahan and Miller reported the result of a splenectomy on a patient

Operation.—On opening the abdomen a large quantity of blood-stained peritoneal effusion escaped. Roughly half-way down the small intestine was a blackened, obviously gangrenous loop of gut, adjoining which was a thick oedematous hard mesenteric mass. A length of gut three feet in length, with as deep a wedge of mesentery as was deemed advisable, was then resected, the line of section being made about 6 in. away from any doubtfully coloured intestine at each end. As the mesentery was cut it was clear that the thrombosis had extended beyond the line of section as clot was extruded from the cut veins.

An end-to-end anastomosis was performed and the gap in the mesentery closed, but in view of the presence of thrombosed veins in the cut edge, it was decided to make an entero-anastomosis between loops above and below the junction to act as a safety valve in case of further infarction.

After operation he was given an intravenous drip of normal saline to which heparin in proportion of 7,500 units to each pint was added. The following morning his condition was quite good, his temperature 99° and his pulse-rate 100.

The heparin was continued in the intravenous drip and was increased to 15,000 units per pint on the second day. On the eighth day a slight oozing of fresh blood from the centre of the abdominal wound appeared and it was thought advisable to stop giving heparin. The bleeding stopped the following day and his convalescence was thereafter uneventful.

The course of intramuscular injections of penicillin, 120,000 units daily, was continued until the twelfth day. His bowels acted with the aid of an olive-oil enema on the third day after operation and thereafter remained regular. He has now resumed his duties and is in normal health.

Suppurative Pylephlebitis with Recovery.—F. D'ABREU, Ch.M., F.R.C.S.

E. C., aged 26, a gunner in the R.A., was admitted on August 21, 1945, to Westminster Hospital (G 7359). His previous history was that in January 1945 he had been admitted to another hospital with an appendix abscess. On February 1 he had an appendicectomy performed with drainage.

On February 15, 1945, he had a left subphrenic abscess drained and a month later developed a left empyema which was successfully treated by aspiration and penicillin replacement.

He was complaining of pain in the upper abdomen with frequent rigors. His temperature was 103° and his pulse 140.

On examination of his abdomen there was an incisional hernia in the R.I.F., which was red and tender. There was more marked tenderness on the right side over the liver area but no rigidity or evidence of general peritonitis. An X-ray showed raising of the diaphragm on both sides with small areas of collapse at the base of both lungs. A diagnosis of right subphrenic abscess was made and on August 22, 1945, a right subcostal incision was made posteriorly after an aspiratory needle had withdrawn pus. On incising the diaphragm no pus was found in the subphrenic space. The peritoneal cavity was discovered to be shut off below by adhesions. A needle was then inserted in the same line as the diagnostic aspiration and pus was found in the liver. An incision was made into an abscess cavity about the size of an orange in the liver substance and some creamy, odourless pus sucked out. A rubber drainage tube was placed into the abscess cavity and the wound closed firmly around this.

Penicillin was given intramuscularly 120,000 units per day and into the tube twice daily, the tube being clipped off after each administration for one hour.

Culture of the pus showed a micro-aerophilic streptococcus, non-hæmolytic and penicillin-sensitive.

Thirteen days after operation his temperature became normal and penicillin was stopped on the sixteenth day.

A week later fever and rigors again set in and a further course of penicillin was given which reduced the temperature after seven days but was continued for twenty days with a daily dosage of 180,000 units.

On October 15, high fever and rigor recommenced, and on October 18 the liver was needled but no pus was found. A third course of penicillin at the same dosage of 180,000 units daily was given by intramuscular drip for seventeen days but the temperature was not affected and on November 10 it was decided to explore the liver by laparotomy. An enormously enlarged liver was found with a hard mass high up in the right lobe. This was explored and a little pus withdrawn from a deep puncture. The mass was considered to be an inflammatory hepatitis and the liver was not incised. A drain was left down to this part of the liver through a stab wound directly over it and another left in the abdominal wound which was then closed. Penicillin was again given by intramuscular drip and after a week pus began to discharge freely through the stab wound and the

P.S.—Since the Clinical Meeting took place, a sternal puncture was performed. This is the result:

					%
Myeloblasts	1	0.3
Premyelocytes	7	2.3
Neutrophil myelocytes	40	13.3
Eosinophil myelocytes	3	1.0
Neutrophil polymorphs	40	13.3
Eosinophil polymorphs	2	0.6
Basophil polymorphs	1	0.3
Lymphocytes	16	5.3
Hæmocyto blasts	1	0.3
Pro-erythroblasts	1	0.3
Basophil normoblasts	32	10.6
Polychromatic normoblasts	126	42.0
Orthochromic normoblasts	28	9.3
Plasma cells	1	0.3
Myeloid erythroblast ratio	1	3.1

The striking feature of this marrow is the very large number of nucleated red cells many of which (5.6% of the total cell count) are in mitosis.

Hæmopoiesis is, however, *normoblastic*.

This seems to be the marrow of a patient responding to increased destruction of red cells.

Therefore, the patient is essentially suffering from a *hæmolytic process*.

Resection of Small Intestine for Mesenteric Venous Thrombosis.—F. D'ABREU, Ch.M., F.R.C.S.

Cases of recovery after resection of the intestine for mesenteric vascular occlusion are rare and are nearly all in arterial embolic cases. Recovery after operation for mesenteric venous thrombosis is extremely uncommon as the trauma consequent to resection, however slight, is likely to produce a further spread of the thrombotic process centrally.

The successful outcome in this case is ascribed to four precautions which were taken to guard against the risk of further infarction: (1) A wide excision was performed with removal of a deep wedge of mesentery. (2) After end-to-end anastomosis of the cut ends, a lateral anastomosis between portions of gut respectively a foot above and below the junction was made to act as a safety valve in the event of thrombosis at the site of the repaired mesenteric gap. (3) Heparin was given intravenously for eight days. (4) Penicillin was administered empirically to deal with any systemic infection causing the thrombophlebitis.

Case Record, Westminster Hospital (G8256).—A Staff Sergeant, age 40, in the Belgian Army, was admitted on September 18, 1945, complaining of a dull heavy pain just below the xiphisternum. This had started suddenly on the morning of September 11, and he had been kept in bed at a Casualty Reception Station. The pain got less but still persisted and he was sent up to Westminster Hospital a week later.

His previous history was of a thrombophlebitis in the left internal saphenous vein just above the knee, after a bruise in that region in October 1944. Whilst in bed with this, he had a severe massive collapse of the right lung from a pulmonary embolus, followed a week later by thrombosis of the right internal saphenous in the thigh. Examination revealed tenderness and resistance in the epigastrium but the rest of the abdomen was normal. No mass could be felt and the abdominal wall moved on respiration. His temperature was 101° and his pulse 80. Blood-pressure 130/80; heart sounds normal. He was obviously in great discomfort, but no definite diagnosis could be made and it was decided to keep him under observation, as a possible subacute pancreatitis or high retro-cæcal abscess.

A white cell count totalled 14,800 per c.mm. His bowels had been constipated before admission but an enema the following morning produced a good result. Gregerson's test of the stool for occult blood was negative. The result of a further enema on the 22nd was also apparently normal. His temperature gradually fell during the next five days, at the end of which it was normal and his pulse 70.

His epigastric resistance had gone but he still complained of epigastric pain and tenderness. On the evening of September 24, the seventh day after admission, he complained that the pain in his abdomen was much worse and his chart showed a gradually rising pulse and a temperature of 99° F. He had vomited and an enema had produced only a small constipated stool of normal colour.

On examination he was resistant and tender all over the abdomen, which was moderately distended. On auscultation no intestinal movements could be heard. A diagnosis of an acute small intestinal obstruction was made and the patient taken to the theatre.

History (9.10.42).—Torpedoed off W. Coast of Africa, subsequently spending two hours in water and ten days in lifeboat. Apparently satisfactory recovery. One month later attack of conjunctivitis, duration one month.

About February 1943 onset of general fatigue and lassitude, followed a few weeks later by aching pains in limbs and back. Symptoms were intermittent, and he remained at work. Started to lose weight about December 1944.

March 1945: Sudden attack of stiffness involving whole body except head and neck. Admitted to hospital and treated as fibrositis without-improvement.

19.10.45: Admitted Archway L.C.C. Hospital. Diagnosis: "Myositis of unknown origin." Eosinophilia suggested trichinosis. X-rays of limbs showed no opacities. No muscle biopsy. Treated with physiotherapy. Condition slowly deteriorated. Soon after admission complained of dimness of vision, followed a few weeks later by thirst and polyuria. Discharged 22.12.45 and admitted to Seaman's Hospital 27.12.45.

Positive findings.—Apathy and profound lassitude. General wasting. Dry, sore tongue. B.P. 190/130. Bilateral diminution of visual acuity, retinal hæmorrhages and exudate. Muscular wasting, poor tone; movement and co-ordination normal. Sensation: Small area of diminished light touch on dorsum of both feet. Absent tendon reflexes. Abdominal reflexes present. Plantars flexor. Heart not enlarged.

Investigations 31.12.45.—X-ray of chest, right leg, skull, nothing abnormal found.

31.12.45: R.B.C. 5,190,000; Hb. 102%; W.B.C. 23,000. Polys. 87%, small lymphos. 11%, large lymphos. 1%, eosinos. 1%. W.R. and Kahn negative. Serum calcium 9.76 mg. %.

1.1.46: Blood urea 47.2 mg. %.

4.1.46: Fæces—no cysts or ova seen.

14.1.46: Blood sugar at 10.15 a.m. 0.156% (not fasting).

Urine: This has been examined daily, and shows a high output of between 200 and 250 oz. of low sp.gr. (av. 1004.5). The output is constantly in excess of the intake. Traces of sugar and scanty hyaline tube casts have been found on two occasions. There are sometimes traces of albumin. Reaction consistently alkaline.

Blood urea 29 mg. per 100 c.c. B.S.R. 11/200 in 1 hour.

Progress.—Following admission condition unchanged. Thirst, polyuria and dimness of vision have been chief symptoms. Backache severe initially but absent recently.

Exhibition of pitressin $\frac{1}{2}$ c.c. b.d. had no therapeutic effect. Restriction of the fluid intake resulted in no greater concentration of urine.

1.2.46: Re-examination showed a faint response of biceps, triceps and supinator jerks on both sides. Faint response both knee-jerks. Ankle-jerks still absent. B.P. 160/130.

Comment.—This patient showed most of the features of periarteritis nodosa but there were no skin nodules. Hypertension without radiological evidence of cardiac enlargement is remarkable. Leucocytosis and fever suggest an infective process. The diagnosis of cysticercosis was also suggested.

POSTSCRIPT.—This patient died on March 1 and autopsy showed hypertrophy of the left ventricle with renal changes characteristic of malignant hypertension.

Chronic Myeloid Leukæmia with a Goitre and Raised B.M.R.—J. S. RICHARDSON, M.V.O., M.D., M.R.C.P.

Ellen M., aged 54, a housewife, was admitted to St. Thomas's Hospital under the care of Professor O. L. V. de Wesselow on 7.11.45.

A swelling in her neck was first noticed about one year before, and a month or so later she noticed that she was short of breath on exertion, and began to experience attacks of palpitations, with a feeling at night as if her heart was beating irregularly. She has never had any anginal or precordial pain and her ankles had not been noticed to swell.

She found that she was getting extremely emotional and nervous at that time and while she was not upset by such warm weather as we had in the summer, she had felt the cold less than usual during the winter months. Her normal weight was 7 st. 5 lb. but she had noticed she had been getting much thinner during the last five months and at the same time she was increasingly tired, and life was more and more of an effort. She had had no dyspepsia and no abdominal pain, but her appetite was very poor. In the past she had had no serious illnesses but she had always been rather nervous.

On examination.—She was extremely thin with a moist skin and bright eyes. There was no tremor of her hands. Weight 5 st. 5 lb. An adenoma of the right lobe of the thyroid gland was present with some diffuse enlargement. Pulse-rate 120. B.P. 180/100. No abnormal physical signs were found in the heart.

Lymph nodes: A few small glands were felt in the neck on the right side and in the left axilla.

abdominal incision. The temperature gradually settled and the penicillin was stopped. The pus again grew the same micro-aerophilic streptococcus.

On November 24 he became tender over the left lobe of the liver after the discharge of pus had ceased and his temperature again rose. On December 3 his abdominal wound again discharged pus and the left-sided tenderness subsided as did his fever.

On December 12 his temperature and pulse again rose and he again complained of pain in the area of the right side of his liver and a resection of a portion of the tenth rib in the post-axillary line was performed. This time a subphrenic abscess was found. For four days before operation and for eight days afterwards he received 400,000 units of penicillin daily by intramuscular drip and 50,000 daily into a tube draining the subphrenic abscess. After this operation and course of penicillin, his temperature and pulse returned to normal and have remained so ever since. He is now ambulatory and in good health.

This patient had two separate large hepatic abscesses in the right lobe seen at operation and almost certainly another large one in the left lobe.

On the advice of Dr. T. L. Hilliard, who gave me valuable help in treating this patient, a course of methionine was given almost throughout his long illness to counteract a probable depression of liver function. This was tested by Dr. N. F. MacLagan on December 7 towards the end of his illness and gave normal results.

This case shows that it is always worth while exploring the abdomen in a case of suppurative pylephlebitis and might show reason for giving greatly increased penicillin dosages where penicillin-sensitive organisms are not easily accessible to the systemic blood supply.

Cesophagectomy for Carcinoma. Restoration of Function by an Ante-thoracic Jejunal Graft.—VERNON C. THOMPSON, F.R.C.S.

E. W. B., male, aged 70. Admitted to hospital 14.5.45.

History.—Six months' increasing dysphagia with retrosternal pain on swallowing.

On examination.—Fairly fit man; chronic bronchitis. B.P. 170/100. Able to swallow semi-solids. Barium swallow showed obstruction at middle third of oesophagus; and a right-sided aorta. Cesophagoscopy: An ulcerated growth 30 cm. from the gums. Biopsy: squamous-celled carcinoma.

19.6.45: *Operation (1).*—A length of jejunum was mobilized according to the technique of Yudin and brought up under the skin to the level of the 2nd rib.

26.8.45: *Operation (2) Cesophagectomy.*—Through a right transpleural approach the oesophagus was removed, the upper end was brought out in the neck and anastomosed to the upper end of the jejunal graft.

Progress.—The end of the oesophageal stump sloughed and the anastomosis broke down; the patient was fed by a drip into the jejunal graft until the ends of oesophagus and jejunum were healthy. The fistula was later closed by a secondary operation. (Fig. 1.)

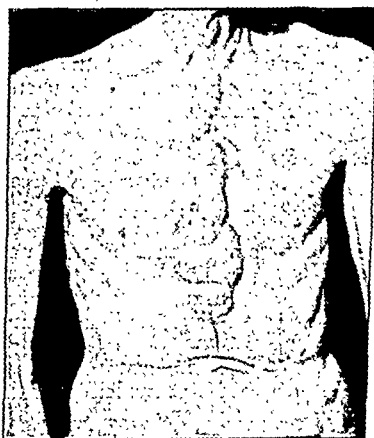


FIG. 1.—E.W.B. Showing ante-thoracic oesophagus made from a jejunal transplant.

Malignant Hypertension.—A. L. WINGFIELD, M.D.

A. M., ship's storekeeper, aged 30. Admitted 27.12.45. Complained of general lassitude, stiffness and aching in limbs, loss of weight, thirst, polyuria, and dimness of vision. Family and previous history non-contributory.

sensitive method they possess of assessing the degree of activity in these cases and their response to treatment (Uhlmann and Goldner, 1944; Krantz and Riddle, 1928).

The B.M.R. in our case was still +28% when the white count had fallen to 13,500 and there were no primitive cells. This might mean that the leukæmia was still active or that she had a coexisting hyperthyroidism.

It is worthy of note in this connexion that there was a large creatinuria and practically no arteriovenous blood sugar difference after an insulin-glucose test, both features of thyrotoxicosis (Griffiths, 1939). The blood iodine and cholesterol are variable in leukæmia (Turner *et al.*, 1940), and were not done. The problem was solved, however, by a further fall in the B.M.R. to +15% with a white cell count of 4,400 cells, 72% polymorphs and no primitive cells.

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Idiopathic Pulmonary Hypertension.—RICHARD F. JARRETT, M.R.C.P. (for MAURICE NELLEN, M.R.C.P., M.R.C.P.Ed.).

Mary O'M., aged 26. This patient was in Hammersmith Hospital from 1.5.45 to 17.5.45 with condition as follows:

History.—One year ago she began to be breathless on exertion and now is breathless after walking quickly on the level. She had never before been breathless on exertion.

Previous history.—Healthy. No rheumatic fever. Normal child life. Two normal pregnancies with healthy children now aged 5 and 2.

Family history.—Healthy.

On examination.—Jugular venous pressure +2.3 cm. Heart: Apex beat $4\frac{1}{2}$ in. in 4th space. Systolic murmur all areas. No thrill. Heaving impulse in 3rd left space 2 in. from midline. P_2 loud. B.P. 114/82.

Investigations.—(1) X-ray: Heart much enlarged. L.V. and R.V. enlarged. Diam. $6\frac{3}{4}$ in. (6 ft. film). (2) Decholin time 12 secs. single end point. (3) E.C.G. marked right preponderance.

Progress.—Much improved by two weeks' rest in bed. She then went home but was unable to do housework because of dyspnoea. In December 1945 first noticed ankles swelling and late December 1945 first noticed neck swelling. At this time fainted twice, once on running upstairs and once after a very hot bath. No cough or hæmoptysis.

Readmitted 9.1.46.

On examination.—Normally developed young woman; moderate cyanosis lips and cheeks; slight icteric-tinged skin; orthopnoea, and dyspnoea on level walking. Oedema of ankles (disappearing with bed rest). Liver enlarged $1\frac{1}{2}$ in. below costal margin, firm and tender. Ascites. Jugular venous pressure +6 cm. Lungs and C.N.S.: normal. No clubbing of fingers. Pulse regular, 80. Heart: A.B. 5 in. in 5th space. Right border $\frac{1}{2}$ in. to right of right sternal margin. Heaving impulse to left of sternum in spaces 2, 3, and 4, max in 3. M_1 loud and sharp. P_2 very loud. A_2 normal. Systolic murmur in spaces 3 to 5 to left of sternum, max. in space 5, not conducted to axilla. No diastolic murmurs. B.P. 110/80.

Investigations.—W.R. and Kahn: negative. Blood-count: R.B.C. 5,500,000; Hb. 114%. Plasma bilirubin 2.3 mg.%. E.C.G.: Right preponderance ++ ($P_2 \uparrow T_2 T_3 \downarrow$). X-ray heart shows slight increase in transverse diameter (now $7\frac{1}{2}$ in.) compared with May 1945. Pulmonary artery more prominent. Ba. swallow: No left auricular enlargement.

Circulatory studies (Dr. Sharpey-Schafer).—Cardiac catheterization showed very greatly raised right auricular and right ventricular pressures and no evidence of left to right or right to left shunt. The arterial oxygen saturation was only slightly reduced. The resting output was moderately reduced.

Treatment.—Bed rest. Pulv. digitalis fol. 1 grain b.d. Mersalyl 2 c.c. twice weekly.

Course.—Slow symptomatic improvement during the past month in hospital.

Differential diagnosis from other causes of right ventricular hypertrophy with right heart failure, which can be excluded as follows:

(A) *Cor pulmonale.*—No clinical or radiological evidence of disease of the bronchi or lung parenchyma.

(B) *Mitral stenosis.*—Persistent absence of mitral diastolic murmur and normal left auricle on barium swallow.

The spleen: The spleen was very greatly enlarged and extended well below but not to the right of the umbilicus. The urine was normal.

Investigation and subsequent course:—B.M.R. +85%. Blood count: red cells 4,100,000; Hb. 62%; W.B.C. 310,000. Polys. 36%. Primitive granulocytes 55%; Transitional myelocytes 17%; Metamyelocytes 7%; Neutrophil myelocytes 31% (lymphocytes 2%). Urinary creatinine 98 mg. for 100 c.c. of urine. Urinary creatine 42 mg. for 100 cc. of urine.

Insulin-glucose test (the arterio-venous blood sugar difference: an indication of peripheral insulin resistance) showed no a-v difference and thus a very high peripheral insulin resistance. Thiouracil, 0.8 gramme daily, was given for four weeks (16.11.45 to 11.12.45) with some subjective improvement but the pulse-rate, the size of the spleen, and weight were unchanged; the B.M.R. was +87%, and the total white cell count 443,000 at the end of the treatment.

Deep X-ray therapy eight applications were then given, the last being on 21.12.45. Anterior and posterior splenic fields were irradiated and a total dosage of 500 r was given to each field. The spleen was very considerably reduced in size, at the end of this treatment, the pulse-rate had dropped to between 90 and 100, her weight was unchanged, the B.M.R. had fallen to +32% and the total white cell count was 100,000.

Polys. 58.5%. Primitive granulocytes 24.5%; transitional myelocytes 7%; metamyelocytes 3%; neutrophil myelocytes 14.5%. Urinary creatinine 1,050 mg. per 100 c.c. urine. Urinary creatine 245 mg. per 100 c.c. urine.

A second course of deep X-rays ended on January 10, 1946, and a total dosage of 200 r was given to both anterior and posterior splenic fields. Following this course the spleen was no longer palpable, the pulse-rate between 70 and 80, the B.M.R. was +32% and the total white count 20,350. Polys. 74%. Primitive granulocytes 6%. All metamyelocytes.

On January 21, 1946, the a-v difference was still minimal and the urinary creatinine 770 mg. per 100 c.c.; urinary creatine 390 mg. per 100 c.c. The B.M.R. was +28%, the leucocyte count 13,500. Polys. 85%. No primitive cells.

On 6.2.46 her B.M.R. was +15% and the leucocyte count 4,400 with 72% polymorphs and no primitive cells. Her general condition was definitely improved and her weight had risen by 3 lb.

A considerable rise in the B.M.R. is commonly found in leukaemia.

Gunderson (1921) reported 19 cases with a variation of +6% to +80% and Minot and Means (1924) found a raised B.M.R. in 72, and showed that the amount of pulse elevation for a given rise in B.M.R. was essentially the same as in hyperthyroidism. They drew attention to the marked clinical similarity between hyperthyroidism and chronic leukaemia particularly in those symptoms that are referable to increased heat production such as an increased tolerance to cold, sweating, loss of weight and dyspnoea.

Friedgood (1932) was even more impressed by the similarity between the two conditions and treated 10 cases of lymphatic leukaemia with Lugol's iodine on the supposition that the fundamental disturbance in both was a hyperactivity of the sympathetic nervous system, and that Lugol's solution acted as a sedative. He claimed a significant reduction in the B.M.R. in 6 of these 10 cases and 4 of these also showed a proportional drop in pulse-rate.

Encouraged by these views Dameshek *et al.* (1934) subjected a woman of 42 with aleukaemic leukaemia to total thyroidectomy four months after Lugol's iodine (10 minims t.d.s.) and two and a half months after deep X-ray therapy to the spleen had failed to reduce the B.M.R. or to alter appreciably the size of the spleen and lymph nodes. They reported a very large reduction in size of the spleen and lymph nodes after operation and found that the lymphoblasts disappeared entirely from the peripheral blood. The B.M.R. fell to -22% in three months and the patient was then given thyroid by mouth. The thyroid gland showed no evidence of hyperplasia and presumably played no part in raising the B.M.R.

This was to be expected as the very high oxygen requirement of the leukaemic cells is regarded as being the cause of the increased metabolism, and the number of primitive cells and the level of the B.M.R. show a direct relationship to each other in most cases (Riddle and Sturgis, 1927). There are, however, instances where this relationship does not appear to exist and a high B.M.R. may be found while the cell count in the peripheral blood is low. An explanation of this may be that the disease is still in an active phase, the blood-forming organs full of primitive cells and the blood free of them by chance. Again a high count may be found in the blood although the B.M.R. has fallen to normal as a result of deep X-ray therapy to the spleen, indicating that sufficient treatment has already been given and that the cells will fall to normal without further treatment. In fact several radiotherapists consider that the B.M.R. is the most

Section of Orthopædics

President—W. B. FOLEY, F.R.C.S.

[December 4, 1945]

Dysplasia Epiphysealis Multiplex

By H. A. T. FAIRBANK, D.S.O., M.S.

CASES in which several epiphyses have shown irregular ossification have been published from time to time under a variety of titles. Some are undoubtedly examples of one or other of the recognized conditions in which changes in some of the epiphyses constitute a minor feature, while others have been described as multiple osteochondritis, with little to support this diagnosis. With pseudo-coxalgia, a typical instance of osteochondritis, these cases show nothing in common except irregular ossification and flattening of the head of the femur. The progressive changes characteristic of pseudo-coxalgia have not been recorded in the cases under discussion.

It is the purpose of this paper to describe the features of a condition which I believe should be regarded as a clinical entity, and as a developmental error resulting from some unknown cause. It is characterized by dwarfism, stubby digits, and mottling or irregularity in density and outline of several of the developing epiphyses, and it lacks the other abnormalities of the skeleton necessary for its allocation to one of the well-recognized groups. As usual, difficulty has been experienced in deciding whether to include an individual case in the group or relegate it to the scrapheap of unclassified cases. Doubtful cases have been excluded.

The following description is founded on the study of 15 cases, 7 of which have already been published, but only 2 of these under the title of this paper. Cases included have been published under the following titles: Achondroplasia (White, 1924); Epiphyseal Dysostosis (Jansen, 1934); Dwarf with Stippled Epiphyses (Buxton, 1930); Hereditary Deforming Dyschondroplasia (Gardiner-Hill, 1937).

In 1935, in discussing the classification of generalized affections of the skeleton, I ventured to suggest Epiphyseal Dysplasia for the title of a group and briefly reported a case. To this Generalisata was added, but this was altered later to Multiplex, as being more accurate. In 1938 cases under this title were shown before this Society (Wiles and Yarrow respectively).

The features of the condition as found in this series are as follows: It is an affection of children and young people: the ages in this series varied from 18 months to 20 years. One of my cases, first seen at 14 years, has been followed for over twenty years.

It affects both sexes and is not inherited as a rule, but one case, a boy, appeared to have inherited it from his mother, while two sisters are included in our series. Intelligence is usually normal. Some degree of dwarfism, of the short-limb type, is the rule, it being definitely recorded in 13 of the cases. Some enlargement of the epiphyses is occasionally

(C) *Congenital heart disease*.—No heart trouble or cyanosis in early life. (1) *Pulmonary stenosis*: No pulmonary systolic murmur or diminution of the pulmonary second sound. (2) *Septal defect*: The circulatory studies exclude any intracardiac shunt.

(D) *Beri-beri*.—There has been no dietary deficiency.

(E) *Ayerza's disease*.—Gross cyanosis and polycythæmia absent, and normal lung shadows on X-ray.

Dr. Terence East (*Brit. Heart J.*, 1940, 2, 189) described three cases which clinically resembled the above, and which on autopsy showed no gross pulmonary endarteritis or other anatomical cause for the pulmonary hypertension.

A Simple Technique for Capillary Microscopy.—ELI DAVIS, M.D.

The technique of capillary microscopy is disarmingly easy. For a good view of nail-bed capillaries a special capillary microscope is unnecessary. Any good laboratory microscope will do, but a binocular instrument has advantages. A powerful light is concentrated by a lens (5x) on to the nail-bed. I use a table which fits snugly over the microscope platform on which the arm and hand are supported. The table is grooved where the fingers rest. The 2/3 objective is used, and a useful magnification is 60. In most patients washing of the nail-bed is unnecessary, and scrubbing must be avoided. The dry nail-bed is covered with immersion oil.

Technique is easy, but interpretation of what is seen requires experience. Age of the patient and the room temperature affect the capillary pattern. There may be marked differences between the capillaries in different fingers, and even in the same nail-bed. A common pitfall is the observation of a number of patients suffering from some particular disease and then deducing that the capillary picture is characteristic of that disease—without sufficient knowledge of possible variations in normal persons, and the appearances in common diseases. It must be remembered that at the nail-bed only a tiny fraction of the body's capillaries can be seen.

But despite these difficulties capillaroscopy is a useful ancillary aid in the study of human physiology and pathology, and in certain conditions gives useful information—for example in the study of petechiæ formation, Raynaud's disease, atheroma, vasomotor instability, and clubbed fingers.

(Capillary microscopy was demonstrated, and representative paintings of appearances were shown. See figures.)

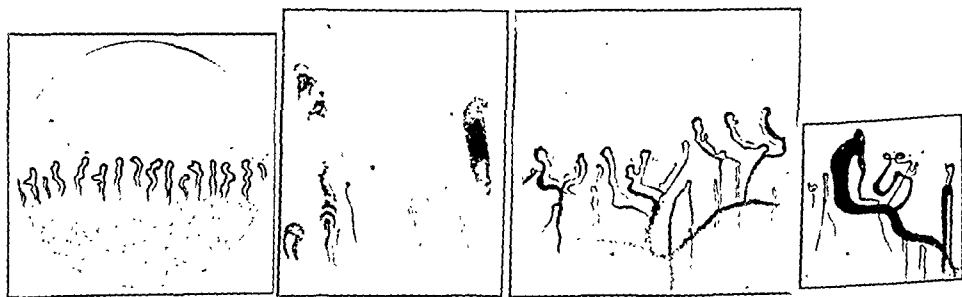


FIG. 1.—Normal capillaries. FIG. 2.—Petechiæ formation. FIG. 3a.—Capillaries in Raynaud's disease. FIG. 3b.—Raynaud's disease. Same patient as in fig. 3a.

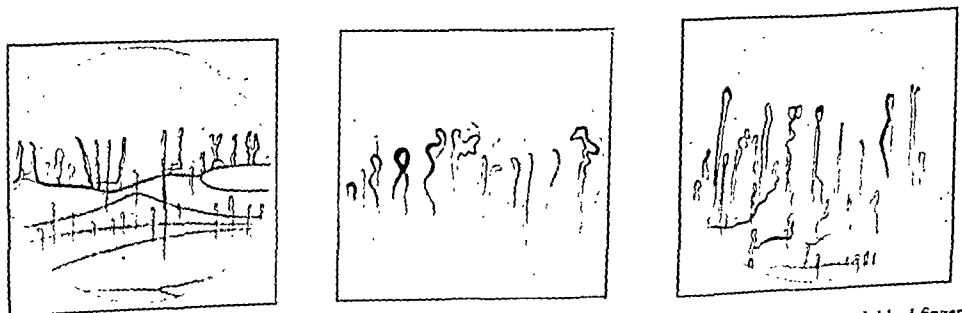


FIG. 4.—Capillaries in atheroma. FIG. 5.—Capillaries in vasomotor instability. FIG. 6.—Capillaries in clubbed fingers. (Paintings by Mr. P. Startup, photographed by Mr. J. E. Andrews. x30.)

Lastly, mottled epiphyses have been described by Traub (1939) in association with pituitary gigantism.

Finally I would suggest that if there is reason to suspect pseudo-coxalgia in a patient below the average in height it is well worth while having films taken of the shoulders and ankles to exclude the developmental error which is the subject of this paper.

I am greatly indebted to friends who have supplied me with details of cases under their care.

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Cerebral Palsy

By E. STANLEY EVANS, F.R.C.S.

It is over one hundred years, namely in 1843, since W. J. Little described in a course of lectures at the Royal Orthopædic Hospital, as it was then called, the condition of spastic rigidity of the limbs of newborn children. The lectures were published in the *Lancet*, and more fully in his book published in 1853, on the "Nature and Treatment of Deformities". In 1861 he read a paper to the Obstetrical Society of London "On the Influence of Abnormal Parturition, Difficult Labours, Premature Births and Asphyxia Neonatorum, on the Mental and Physical Condition of the Child especially in relation to Deformities". In less than twenty years in orthopædic practice alone, and here it will be remembered that Little was a physician to the London Hospital, he saw about 200 cases of spastic rigidity excluding idiots in asylums. He dealt at length with the ætiology of the condition, his description of patients suffering from Little's disease was graphic and has never been surpassed, and he laid down certain precise principles of treatment. Although in speaking to the obstetricians he stressed the importance of birth injuries and of neo-natal abnormality, yet in addressing his students of orthopædy he stressed his belief in the pre-natal lack of development of the brain in these cases. Stewart, in his Presidential address to the Neurological Section of this Society, in 1942,¹ emphasized his view that there was no single and specific cause of cerebral diplegia, that birth injury had in the past been assigned too large a part in the pathogenesis, and that the most common cause was primary degeneration of the cerebral neurones as suggested by Collier.

Little gave admirable descriptions of his cases and stressed the frequency of mental impairment, of speech defects, of difficulties in feeding and swallowing, of functional disability of the upper limbs, of constipation and of the typical deformities in the lower limbs. He recognized the association between hemiplegia and epilepsy and realized that mild cases might exhibit no manifestation other than awkwardness, and that in many the intellect was unimpaired.

In his treatment of these patients Little was essentially conservative, and used tenotomy only as a last resort. This is the more interesting when it is remembered that Little introduced the operation of subcutaneous tenotomy into this country after Stromeyer had operated on him with great benefit for the club foot from which he suffered.

Since that time children suffering from Little's disease have usually been passed by the pædiatricians and neurologists to the orthopædic surgeon. The surgeon often performs tenotomies or neurectomies in an attempt to establish muscle balance and thereby still further weakens the limb. This treatment is preceded and followed by physiotherapy and walking exercises. In the orthopædic hospital school attempts are made to educate these children and I think it is true to say that the physiotherapists, school teachers and even the surgeons have often been pessimistic as to the outlook and disappointed with the results, and the question has often been asked: "Are these children worth all the effort and money spent on them?" Here was Little's answer: "I have had many cases under observation from one to twenty years and may mention as an encouragement to other

¹*Proc. R. Soc. Med.*, **36**, 25.

seen. The hands are striking, the fingers and thumbs being short, thick and stubby with blunt ends. Apart from the dwarfism and the shape of the hands, there is no characteristic deformity, but the following were noted: Flexion contracture of some of the joints—knees, elbows and hips—has been present in a few cases, and in one limitation of abduction of the shoulders. In single cases, subluxation of the radial and of the tibial heads was noted. The spine is usually free from deformity. Difficulty in walking or pain and stiffness, particularly of the knees, has been present in several cases.

Radiological findings.—The essential abnormalities are seen in the epiphyses, the centres for which may be late in appearing, backward in development, and slow in fusing with the shafts, but the principal change is irregularity in ossification. They are irregular both in density and shape, being mottled in appearance and perhaps mulberry-like in outline. Separate subsidiary centres around the main centre are common, and this results in some peripheral stippling. There is a definite tendency toward improvement, the epiphyses eventually becoming normal in density, but not in outline, which, though smooth, remains permanently abnormal. Any or all of the epiphyses may be affected, the most common to show typical changes and permanent deformity being the hips, shoulders, ankles and less frequently the knees. The heads of the femora and humeri remain shallow and less convex than the normal. In one typical case the femoral heads at the age of 27 still showed irregularity in outline and partial fragmentation, a condition that might well be mistaken for pseudo-coxalgia, which was in fact the diagnosis made when he was first seen at the age of 14. The femoral neck may or may not be thickened. Some irregularity of the acetabula was present in only 3 cases.

The femoral condyles may show little in the way of abnormal ossification or the changes may be much more marked. In older children striking irregularity in shape is seen in some cases, the condyles being flattened, and inclined to be rectangular in shape. The patella may show decided mottling.

The ankles show changes of diagnostic value. A slight amount of obliquity of the joint is met with occasionally in normal individuals, but in this condition the obliquity is marked. The lower tibial epiphyses diminish markedly in depth from within outwards. The joint line is therefore oblique, and the trochlear portion of the astragalus is misshapen to conform to this.

In 2 cases the capitellum in each elbow shows as a poorly calcified centre with a sharply defined nucleus of much greater density. The metaphyses show no consistent characteristic change, but they may be trumpeted, and the epiphyseal lines irregular. In 1 case the upper humeral epiphysis, very fragmented and irregular, overlapped the neck on the inner side, while the epiphysis for the tibial head lay in an oblique antero-posterior plane, the tibia being subluxated backwards.

The shafts of the long bones are shorter than normal but not thickened as a rule. The carpal and tarsal bones ossify late, and may be very irregular in outline. The metacarpals, metatarsals and phalanges are stunted. The vertebral bodies show no peculiarities as a rule.

The pathology is obscure.

Differential diagnosis.—There are at least seven other conditions, besides osteochondritis, in which the epiphyses may show irregular ossification. The classical signs of cretinism, the first to be excluded, are absent, and there is no improvement in the appearance of the epiphyses in response to treatment.

In dysplasia epiphysealis punctata, as it is now called, or stippled epiphyses, the whole of an epiphysis seems to be ossifying from a large number of discrete centres. The shafts of the bones are short and thick, and the ends splayed. The tarsal bones may be completely stippled. The abnormalities generally are much more gross than in most cases of the multiplex group.

In chondro-osteo-dysplasia of the Morquio-Brailsford type, the femoral heads show striking epiphyseal changes but in this condition the acetabula are markedly enlarged and irregular. Notable features are the abrupt kyphotic deformity in the dorsolumbar region, and the shape of the vertebral bodies; in the latter the central prolongation anteriorly is quite distinctive and diagnostic.

In dyschondroplasia changes in the epiphyses, when seen, are completely overshadowed by the gross abnormality of the metaphyses: they are never seen except when the adjacent portion of the metaphysis contains obvious masses of cartilage.

In osteopetrosis or marble bones, some of the epiphyses may show irregular density or stippling, but the changes in the shafts dominate the picture.

re-training of muscles and improved joint mobility must be sought and attained. Exercises must be graded very carefully until the patient can use the spastic muscles without the development of the spastic stretch reflex and the tone of the weak muscles must be improved. In Phelps' view, operation should only be carried out when structural contractures are present. Little practically enunciated the same principles. It is essential in apathy to gain and maintain a full range of joint movement.

In athetosis the essential element is to train for conscious and voluntary relaxation by Jacobson's methods and to assist in eliminating purposeless movements. In athetoid quadriplegia with tension the attainment of relaxation releases the tension and the athetoid movements become evident. In all doubtful cases this therapeutic test is invaluable in establishing the diagnosis. Ultimately the patient should be able to relax in all positions, starting flat, then on a reclining couch, sitting on a special relaxation chair and so on, and all movements must be carried out with a minimum expenditure of energy from the relaxed position. Records showing progress are kept in the form of graphs.

In the treatment of these children suffering from cerebral palsy, a wide and comprehensive approach from all angles is essential, and treatment must be individual, intensive and progressive. In a Unit such as the one at Carshalton the services of a physiotherapist, occupational therapist, speech trainer, educational psychologist and a school teacher, highly skilled in their several spheres of therapy and conscious of each other's problems, are available. The patients are discussed at a weekly conference of all the therapists, and each must cope with the individual child at the stage and level he has attained. Collectively they must prepare the child physically and mentally so that he can benefit by education, and the school teacher, for example, must not demand of the child a greater effort and standard than that of which he is capable at any particular moment. Periodic (three-monthly) functional joint and muscle examinations are made, and accurate records kept.

In the attainment of all normal skills, gradual progression is essential. Bad habits have to be unlearned and the children trained to acquire the skills in a manner similar to the development of the normal child from infancy, bearing in mind the motor handicap and the absence of the usual sensory and motor experiences of the child suffering from cerebral palsy. For example, in the case of an athetoid child who has to be taught to feed himself reasonably well, conscious relaxation is essential and all movements are performed from the position and state of relaxation. Ultimately the child sits in a relaxation chair with a felt seat, a foot rest and side arms to give security, at a table with a feeding board made with troughs into which a plate and tumbler fit securely, and is assisted in feeding himself with a minimum of effort. He then progresses to use himself a specially adapted spoon, easy to grip and later to use a similar knife and fork. Training is finally completed when a child is able to sit in an ordinary chair, at an ordinary table and use ordinary cutlery.

The same progressive training is necessary in acquiring the skill of walking. Conscious relaxation in all its stages is necessary, and ultimately the child is made to stand in boots fixed to specially weighted skis with poles. The weights, and later the poles, are removed, and the child stands and walks in skis alone. Training is ultimately successful if and when the child is able to stand and walk, for increasing periods, in ordinary boots.

[The type of ski used was shown to the meeting.]

In speech training, progression implies relaxation and correct breathing, vowel production, production of the easiest, and later the most difficult consonants, followed by simple word production. A child satisfactorily rehabilitated can walk and talk at the same time, but it must be remembered that the performance of a double skill at one and the same time represents very considerable attainment. This training will produce results in the educable and co-operative child but no length of treatment can be laid down, as each individual varies in his initial handicap and in his rate of progress. I have not referred to the medical personnel of such a unit but there should at least be a neurologist, a psychiatrist, a paediatrician and an orthopædic surgeon. Operative trauma or therapy should be reduced to a minimum.

50 patients suffering from cerebral palsy have been seen during the past few months, and 22 of these have received, or are receiving, treatment in the Unit. Of the 50 all but 4 had been diagnosed as suffering from spastic disease, and the 4 from various forms of chorea. 25 of the 50 patients were found to be educable athetoids and there were only 2 ineducable athetoids. There were 7 educable spastics only and 13 ineducable spastics. 2 patients were found not to be suffering from cerebral palsy and in 1 the differentiation

practitioners that treatment based upon physiology and rational therapeutics affects an amelioration surprising to those who have not watched such cases. Many of the most helpless have been restored to considerable activity and enjoyment of life."

At Carshalton, where for many years we have been constrained to take these children, much thought and treatment has been expended on them. It was felt to be unwise to segregate them in one or more wards and so they were parcelled out amongst the wards, the physiotherapists and the teachers. The teachers regarded them as an encumbrance and felt in practically all cases that they held back the rest of the class. The children were regarded generally as mentally retarded, were kept in a corner of the ward and given walking exercises, neurectomies and more walking exercises, and the results were most disappointing. Satisfaction was experienced when a child acquired a good stance and was enabled to walk reasonably well. Some did better, or less badly, than others, and a poor result was generally attributed to the lack of co-operation on the part of the mentally retarded patient.

It was with this background that some three years ago I appointed Mrs. Collis as a physiotherapist dealing solely with the spastic child. She is a trained physiotherapist and occupational therapist and had worked with Dr. Winthrop Phelps at Baltimore.

In the Cerebral Palsy Unit at Carshalton we have applied the principles enunciated by Winthrop Phelps and so far as practicable carried out the appropriate regime of treatment.

For over twenty years Phelps has had a remedial school for spastics, and as the result of his researches and experience insists in brief on: (1) an accurate diagnosis of the condition; (2) a careful mental assessment; (3) a wide, comprehensive and intensive approach so far as appropriate treatment is concerned.

His classification on a motor basis of patients suffering from cerebral palsy is: (1) spasticity (quadriplegia, monoplegia, hemiplegia); (2) athetosis; (3) ataxia; (4) tremor; (5) rigidity.

Spasticity, so far as cerebral palsy is concerned, results from a lesion of the cerebral cortex. Spasticity is constant and is the result of hyper-irritability of the spastic muscle to all stimuli. The essential underlying phenomenon is the spastic stretch reflex, which is the uncontrollable contraction of a spastic muscle when its antagonist attempts to contract. I need not enumerate the clinical features.

Athetosis is the result of a lesion of the basal ganglia and the involuntary movements interfere with normal movements. Phelps subdivides this group into non-tension and tension athetosis. We are all familiar with non-tension athetosis in which the involuntary irregular movements are either rapid or wormlike. In tension athetosis, tension develops secondarily in an attempt to control the athetoid movements—at first voluntary, the tension later become habitual. Tension is usually mistaken for spasticity but there is no spastic stretch reflex. To all intents and purposes the child suffering from athetoid quadriplegia with tension is indistinguishable from the child suffering from spastic quadriplegia unless the condition is sought and recognized. It is vitally important to make this distinction because the treatment and prognosis are different. In our small series, over 50% of patients labelled "spastics" have been found to be suffering from athetosis with tension.

In spastic diplegia there is more likelihood of mental retardation because the lesion is in the cerebral cortex, whereas in athetoid quadriplegia with tension, the lesion is in the basal ganglia and the great majority of the patients are of reasonable or average mentality. It must be remembered that the usual intelligence tests, for example the Stanford-Binet tests, require language and motor skill and due allowance must be made, by the psychologist who understands cerebral palsy, for the difficulties inseparable from the severe motor handicap. The object of mental assessment is to estimate how far a child suffering from cerebral palsy is trainable and teachable. At Carshalton, less than 10% of the athetoids and over 60% of the spastics were found to be ineducable.

The purpose of treatment is (1) to estimate economic potentiality, (2) to make the child independent or semi-independent. Even if unable to earn his own living the patient suffering from cerebral palsy should be able to care for himself and care for his personal needs. Stress is laid on speech training as a means of communication, on hand and arm usefulness, on locomotion and on personal appearance so that the patient may become socially presentable. I cannot, in this short paper, deal with the details of treatment but can only stress certain features.

In spasticity too much attention should not be focused on the spastic muscles, for others are found to be weak and some flaccid. Conscious and voluntary relaxation, the specific

TREATMENT

These cases all came under my care at the Kettering General Hospital, and it was fortunate that I was able to see them on, or soon after, admission.

CASE I.—A farm labourer, aged 56. His accident occurred in December, 1944. He had a very swollen knee-joint.

He was not very shocked and I was soon able to take him to the theatre. A Kirschner wire was inserted into the upper end of the tibia, and manual traction applied. An Esmarch's bandage was then applied to compress the condyles into position. After this was removed it was replaced by a pressure bandage with wool. The extension was tied to the end of a Thomas' splint, which was slung up on a Balkan beam on his return to the ward.

This was left for six weeks, and then the wire was removed and replaced by a strapping extension with the leg straight for a further period of six weeks. He was then given a walking caliper and allowed to go home. There was no movement in the knee-joint.

He attended a class for knee exercises for many weeks but without result, and I had expected his knee to be full of adhesions so I was not disappointed. He stopped attending about last June, but he has come up to see me when I have specially sent for him. His end-result is a stiff stable knee.

CASE II.—This was a girl, a clerk aged 22, and she was admitted on June 3, 1945. Her fracture was compound, but her general condition was good.

Within an hour of admission, the leg was cleaned up and a Thomas' splint was slid up the leg. A strapping extension was then applied below the knee, and the area of operation carefully prepared. I commenced by nibbling away the dirty end of the shaft of the femur, and then manual extension was applied. The wound was dealt with in the usual manner, all damaged muscle being excised. The condyles were much more comminuted than would appear from the X-ray films [shown], but they were put in as good a position as I could obtain, the wound dusted with sulphanilamide powder, and lightly packed with vaseline gauze, and a dressing applied. I had considered putting in a long screw to fix the condyles, but I could not see that any screw could have got a satisfactory hold in such a comminuted bone; and anyway I was opposed to putting any screw into such a wound if it could be avoided. A plaster cast was then applied over the dressing with light wool padding from the ankle to the groin. A window was cut in the plaster for subsequent removal. The extension was transferred to the splint and the splint slung up on a Balkan beam on return to the ward.

She was given 15,000 units of penicillin every three hours intramuscularly for the next five days, and she was fairly comfortable. At the end of a week I again took her to the theatre without disturbing the splint, and under pentothal anaesthesia removed the window and inspected the wound, and found that it looked healthy. A swab was taken and it was sterile on culture. As much as possible of the wound was drawn together with silk worm sutures, but no tension was applied. Again a week later I took her to the theatre and again took a swab, which proved sterile. I removed the sutures and put a split skin graft into the remaining part of the wound. When again inspected in ten days the wound was healed, except for a slight serous discharge from the depression.

This patient did run a slight pyrexia for almost six weeks, but the temperature was never over 100°, and her general condition was excellent all the time. Extension was maintained for twelve weeks, and then she was given a light plaster with a walking caliper. She is still wearing the caliper and she is quite comfortable in it, but she has some pain if she tries to leave it off. Her knee-joint has a few degrees of flexion, and she has not the power of complete extension, and she has some lateral instability.

CASE III.—A Land Army girl aged 19, admitted on June 16, 1945. The wound was almost identical with the previous case, and she was given exactly the same treatment. Her wound was quite dry and healed in three weeks, and she never showed any pyrexia. Though the reduction shown in her films would lead one to expect a poor result, she has the better knee of the two. The film also showed a transverse fracture of the patella low down.

She is regaining a fair degree of flexion and she has a slight medial instability, but she is able to walk quite well without her caliper, and without any discomfort.

CONCLUSION

These cases illustrate what we may call a typical "Pillion Fracture". The treatment carried out illustrates the value of the recent advances in technique—careful wound toilet, penicillin, and early closure by secondary suture and/or skin graft—so reducing what was once a formidable compound fracture to a routine procedure.

I am not, however, trying to demonstrate the correct treatment and reduction of the fracture, or brilliant end-results.

It was my privilege to take part in an orthopædic team under the E.M.S. following the invasion of Europe, and I would like to express my acknowledgment and gratitude to all those who have been responsible for our modern conception of treating compound injuries. I wish also to express my thanks to our Consulting Orthopædic Surgeon, Mr. Leslie Morris, of Leicester.

between spasticity and athetosis with tension could not be made until the child had been under observation for several weeks.

Of the results, I can at present say but little, because an assessment committee of experts is reviewing the value of the work, but I can say that in my view the results have far exceeded my expectations and are better than I personally could have obtained by orthodox methods.

CONCLUSIONS

In order to obtain the optimum results in dealing with children suffering from cerebral palsy the following factors should be borne in mind.

(1) An accurate diagnosis must be made particularly to ensure that patients suffering from athetoid quadriplegia with tension are not confused with those suffering from spastic disease.

(2) A careful mental assessment must be carried out in order to exclude those patients who are ineducable. Some by virtue of mental impairment or because of very severe motor handicap will be capable of partial rehabilitation only.

(3) Generally, the younger the patient the better the prognosis. The 8 months' old infant has less to unlearn and will make more rapid progress, other things being equal.

(4) Operative treatment, in Phelps' view, should be confined to the release of structural contractures in spastic cases, and should not be carried out in patients suffering from athetosis with tension.

(5) Epilepsy is of serious import and such patients should be excluded.

(6) Complete comprehensive and intensive treatment should be carried out in the selected cases, selected because they are educable and not because they have slight motor handicap. Co-ordination of effort between the physiotherapist, occupational therapist, speech trainer, school teacher, psychologist and the medical personnel is essential.

(7) There are thousands of children suffering from cerebral palsy in this country and the time is ripe for the establishment of a number of residential remedial schools as trained staff become available. These must be primarily *not* educational establishments, but centres where children suffering from cerebral palsy can be treated and trained from the physical and mental aspects, and be prepared to such a stage of rehabilitation, that they can benefit by education.

Finally, I must express my appreciation of the work done in this Unit by Mrs. Collis and by Dr. Winthrop Phelps whose principles and practice have, so far as possible, been followed.

Pillion Fractures

By FRANK RADCLIFFE, F.R.C.S.

PILLION fracture is a comminuted T-shaped fracture of the lower end of the femur, with separation of the condyles, and displacement of the condyles behind the shaft of the femur. Recently I have had 3 cases of these fractures all of which occurred in the knees of pillion riders.

In the first case, which was a closed fracture, the shaft was displaced down between the condyles and it was not far from the articular surface of the tibia. In the other two there was a fairly extensive wound with the end of the shaft protruding through the skin and lying over the patella.

Mechanism.—The three accidents all occurred the same way, that is to say, motor cycle and pillion rider being involved with a motor lorry in collision, and by coincidence, in the second and third case with a petrol tanker. As far as I can say the motor cycle had almost avoided the lorry on rounding a corner when the knee of the pillion rider, in a typical position that I need hardly describe, took the whole weight of the impact.

I suggest that the force came against the patella, which was driven almost like a wedge against the condyles of the femur, splitting them apart and detaching them from the shaft, and then the leg, knee, and condyles were driven up under the shaft.

Section of Epidemiology and State Medicine

President—P. G. STOCK, C.B., C.B.E., F.R.C.P., D.P.H.

[November 23, 1945]

The Epidemiology of the 1945 Outbreak of Poliomyelitis in Mauritius [Summary]

By ALLAN M. MCFARLAN, M.A., M.B., B.Chir.

Emergency Public Health Laboratory Service, Cambridge

DURING the first five months of 1945 there were at least 1,018 cases of poliomyelitis in Mauritius. The attack rate was 2.4 per 1,000 of population. In 851 cases there were 64% under 5 years of age and 95% under 10. Only some 4% of the cases were without definite paralysis. In 86% the legs were affected. The dromedary type of temperature curve was present in some cases, and the suggestion is made that the first rise of temperature may correspond to an illness of infection and a period of infectivity.

The epidemic began in February, shortly after a cyclone had caused widespread damage to houses. There was an increasing prevalence of intestinal diseases at the time and it is suggested that the virus of poliomyelitis during passage from a few sporadic cases which occurred in January or from symptomless excretors underwent a mutation and became more invasive and more pathogenic.

The weekly incidence of cases showed a very symmetrical and somewhat steep curve resembling that of an influenza epidemic. The character of the curve suggested an infection with a very short incubation period and a high degree of infectivity. Paralytic poliomyelitis does not have these characteristics, but they might apply to a carrier epidemic of the virus. A short period of infectivity in carriers beginning two or three days after infection would lead to an epidemic curve of the explosive type and the much smaller but similarly explosive curve of cases of paralysis would follow a week or ten days later. Casual contact apparently sufficed to transmit infection, and for this and other reasons the presence of the virus in the pharynx may be more important for the spread of infection than its presence in faeces.

The outbreak was at first localized to one area but spread rapidly all over the island. The spread from place to place appeared in a number of instances to be by healthy adult male carriers. Subsequent spread was mainly by further carriers both adults and school children. Sanitary arrangements were very bad, particularly after the cyclones, and flies were abundant, so that flies might have transmitted infection to a few cases. Only one village had an explosive type of epidemic and there the contamination of ices possibly played a part in the spread of infection. In other villages the type of epidemic suggested a spread by transient carriers.

An Analysis of the Failures of the Smith-Petersen Operation for Fracture of the Femoral Neck

By G. O. TIPPETT, F.R.C.S.

THE speaker described briefly his treatment for these cases of fractured neck of the femur. In the series under review all the cases had been subjected to operation during the period of the last two years. They were divided for purposes of treatment into age groups of over 70 and under 70. In the over-70 group the patients were often severely shocked by the trauma of the injury and unless quickly freed from pain and got out of bed they became bedridden with a poor prognosis of life. In these cases he inserted a Smith-Petersen nail only. He stated that often he inserted a long nail which might protrude through the head of the femur for about a quarter of an inch. If this protrusion was low down on the head, the hip was not arthrodesed and surprisingly little pain resulted. The advantage of this long nail was to secure the maximum grip on the small central fragment of the fracture, so that the patient could be sat up right away and got out of bed within a few days sitting in a chair or walking with crutches. He advocated this measure as a life-saving measure without thought of damage to the joint. For those cases under 70 he performed a Smith-Petersen nailing together with a fibular graft. The advantage of this procedure was that one got a double hold on the fracture fragments. The causes of failure were: (1) due to the fracture itself, and (2) due to the treatment. In (1) the fracture occurred nearly always in later life with inevitable shock. In (2) the failures could be divided into avoidable and unavoidable. The avoidable failures were produced by (a) sepsis, introduced at the time of the operation or late autogenous sepsis giving rise to infection of the hæmatoma or round the nail after some months. (b) Poor placing of the nail. He stressed that the nail must be placed in perfect position with perfect centralization of the nail as shown in two planes by the X-ray films. This was especially necessary when the nail was accompanied by a graft. (c) Extrusion of the nail. This might be a normal process due to shortening of the neck owing to further impaction during the process of union of the fracture, and thus the speaker deprecated the use of a nail with a cross-pin in its base as this held open the fracture line. (d) Avascular necrosis of the head of the femur. This might be due to roughness of the surgeon in reducing the fracture or to damage caused by the mechanical instruments perforating the neck and head of the bone during his operation of nailing. Likewise too early a weight-bearing may damage a head the vitality of which is only just secure, but which would have lived if the trauma of weight-bearing had not been added at too early a date. The unavoidable cases are those of avascular necrosis outside the ability of the surgeon to prevent. In these cases it was part of the penalty of breaking a bone at a site where nature had given a poor blood supply, and death was from shock and old age.

The speaker illustrated these causes of failure by quoting a series of cases that had come into his clinic during the last two years both from his own operating and those of other surgeons. X-rays were shown to illustrate the points.

tion, for example, can be related to the feeding of babies and animals; respiration to ventilation; and reproduction to pets. At this stage, too, health teaching can be illustrated and health morals drawn from the lives of the great.

Between the years of roughly 11 to 16, factual human biology should be the background of health education. *Homo sapiens* will be much more interesting at this stage than the amoeba. Sex instruction must not be omitted, of course, but there should be no over-emphasis of it. The reproductive system and the function of reproduction should be considered as a part of the structure and functions of the body as a whole. In addition to this *ad hoc* health instruction, health teaching should permeate every other subject. For instance, the class might study the history of the growth of the health services; school outings might include visits to see the health services at work. A visit to the sewage farm is surely no less important than a visit to a museum; and discussions on the work of the school doctor and the school dentist and the contribution that they can make to health can be tied up with their visit to the school.

The health education of the adult is the most difficult of all. Old wives' tales have to be debunked and faith in the bottle of medicine shaken. Although we may deplore the interest in disease, we must try to make use of it. For the present generation of adults, therefore, we must often start off our teaching from this interest, teaching physiology under the guise of pathology.

The material we use to assist us in our health education work must be carefully related to our purpose. The leaflet and poster are much less effective than the film, which makes a direct appeal to every section of the community. In the early stages of health education films, there was an attempt—often a somewhat heavy attempt—to create a melodramatic story. The more recent trend is towards a straightforward presentation of health facts which are themselves of sufficient interest to hold the attention of the audience. This move is in the right direction. Exhibitions can attract large numbers of people but it is doubtful if they really change habits or attitudes. They warm the feet but not the heart. There is an immense ready-made audience for health education in our factories and this is a field which should be increasingly cultivated in the future. The lecture carries a direct message, personally delivered, and offers an opportunity for answering questions. Its great disadvantage is that it attracts the converted. The lecture too is sometimes less effective than it might be because the lecturer is often a crank. It is essential that health lecturers should be notably sane. Their lectures should be clearly based upon a wise and common-sense philosophy, and there should be no sign of exaggeration or undue bias.

The most effective health education is personal health education passed on by direct contact. The doctor, the teacher and the health visitor have a great opportunity here. All three, however, have much to learn about the content and methods of health education if they are to play their potential part to the full. The training of the doctor and nurse in the past has itself been much more concerned with disease than with health and most of us would find ourselves hard-pressed to enumerate more than a few health principles. We must build up our knowledge of the physiology of healthy living until it surpasses our knowledge of pathology, and we must see that it is passed on to all those people who are in positions of authority. We must learn too how we ourselves can put this knowledge across in an interesting and inspiring way to those whom we are in a position to influence.

The radio is a health education medium of importance. Only a few facts should be included in each talk and these should preferably have some direct bearing upon the lives of the hearers. The talk that is overcrowded with facts will fail to strike home. A short talk is better than a long one. The appeal to the hearer should be personal and the language simple, straightforward and unadorned. The possibility of misinterpretation should never be forgotten. In this sense the spoken word is more dangerous than the written because one cannot turn back to see exactly what was said. If the radio talk is to be lively and direct it must be dictated and not written. The talk that is laboriously produced in polished writing will not read well on the radio, but will seem stiff and stilted and will make real contact with the audience impossible.

If health education is to develop as it should, it must have the right set-up and machinery. This is a field where voluntary or quasi-official organizations can do better work than Government Departments. The war has shown that people are

The most important factor determining infection was contact. Families with a case of poliomyelitis had a higher percentage of adult males in occupations with contacts outside the village than did the population of the district as a whole, and also a higher percentage of children attending school. In rural districts the attack rates increased with increasing population density. Attack rates were higher in boys than in girls particularly in towns; in Chinese children than in Indian children; in persons in the same family than in the general population. The chances of exposure were greater in the groups with the higher attack rates.

Recent American work has shown that the distribution of faecal excretors of virus during an epidemic is concentrated around cases, as would be expected from faecal spread. However, the distribution of cases of poliomyelitis in Mauritius and in other epidemics has been more diffuse and suggestive of a spread by pharyngeal secretions. At present the measures taken to limit the spread of poliomyelitis should be those used in meningococcal meningitis to prevent respiratory spread and also those used in Sonne dysentery to prevent faecal spread.

The work reported here was done in collaboration with Professor H. J. Seddon and Major G. W. A. Dick, R.A.M.C.

[January 25, 1946]

Popular Health Education

By CHARLES HILL, M.A., M.D., D.P.H.

HEALTH Education must take account of existing prejudices and resistances. It is unfortunate but true that the public is more interested in disease than in health; that it would rather put its faith in a bottle of medicine to cure disease than make the adjustments of life that are necessary to improve health; and that it prefers to be guided in its approach to health and disease by the old wives' tales picked up during childhood than by the latest scientific knowledge. In general, there is a profound ignorance of the working of the human body and any knowledge of physiology which is possessed is drawn almost entirely from patent medicine advertisements, which introduce the public to such physiological truths as the "acid in your stomach will burn a hole in the carpet" and to the concept of "night starvation". As a consequence of these attitudes and influences, the middle-aged are fixed in their habits and encrusted in an almost impermeable shell of folk-lore. To get results, therefore, we must concentrate on teaching the young the healthy habits and the knowledge that can be for them the basis of their healthy living.

In teaching the young there are certain principles that must be borne in mind. Perhaps the most important, and probably the most universally disregarded, is that parents should answer the questions of their children truthfully and without any signs of embarrassment. The fact that a child asks a question on any matter is a sign not only that he is interested—which will, of course, mean that he is also receptive—but that he is intellectually ready to receive the information for which he asks. If, therefore, his questions are answered as they arise—no more but no less—his health education, including his sex education, will proceed in a natural manner. Of course it is desirable that the essential biological facts should be taught systematically as well, and the facts of reproduction should certainly be taught as part of biology before the age of 12. In this way they will become an accepted part of the child's background of knowledge before he has become himself emotionally involved. At all costs, we must avoid making health education appear a set of dreary "don'ts". Our approach must be the inspiring one of stressing the beauty, grace and joy of a positive attitude to health.

Our health teaching must be graded to suit the intellectual level of the people taught. In the case of a pre-school child and a young child up to the age of, say, 7 years, we should be content to teach the proper habits without explanations unless, of course, explanations are asked for. At this stage it is more important for the child to learn to do the right thing, even imperfectly, as a routine part of life than to be expert in and knowledgeable about the right method of doing it. During the next four years or so up to the age of about 11 there should be a gradual development of factual biological teaching based upon the natural interests of the child. Teaching of nutri-

tion, for example, can be related to the feeding of babies and animals; respiration to ventilation; and reproduction to pets. At this stage, too, health teaching can be illustrated and health morals drawn from the lives of the great.

Between the years of roughly 11 to 16, factual human biology should be the background of health education. *Homo sapiens* will be much more interesting at this stage than the *amœba*. Sex instruction must not be omitted, of course, but there should be no over-emphasis of it. The reproductive system and the function of reproduction should be considered as a part of the structure and functions of the body as a whole. In addition to this *ad hoc* health instruction, health teaching should permeate every other subject. For instance, the class might study the history of the growth of the health services; school outings might include visits to see the health services at work. A visit to the sewage farm is surely no less important than a visit to a museum; and discussions on the work of the school doctor and the school dentist and the contribution that they can make to health can be tied up with their visit to the school.

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The material we use to assist us in our health education work must be carefully related to our purpose. The leaflet and poster are much less effective than the film, which makes a direct appeal to every section of the community. In the early stages of health education films, there was an attempt—often a somewhat heavy attempt—to create a melodramatic story. The more recent trend is towards a straightforward presentation of health facts which are themselves of sufficient interest to hold the attention of the audience. This move is in the right direction. Exhibitions can attract large numbers of people but it is doubtful if they really change habits or attitudes. They warm the feet but not the heart. There is an immense ready-made audience for health education in our factories and this is a field which should be increasingly cultivated in the future. The lecture carries a direct message, personally delivered, and offers an opportunity for answering questions. Its great disadvantage is that it attracts the converted. The lecture too is sometimes less effective than it might be because the lecturer is often a crank. It is essential that health lecturers should be notably sane. Their lectures should be clearly based upon a wise and common-sense philosophy, and there should be no sign of exaggeration or undue bias.

The most effective health education is personal health education passed on by direct contact. The doctor, the teacher and the health visitor have a great opportunity here. All three, however, have much to learn about the content and methods of health education if they are to play their potential part to the full. The training of the doctor and nurse in the past has itself been much more concerned with disease than with health and most of us would find ourselves hard-pressed to enumerate more than a few health principles. We must build up our knowledge of the physiology of healthy living until it surpasses our knowledge of pathology, and we must see that it is passed on to all those people who are in positions of authority. We must learn too how we ourselves can put this knowledge across in an interesting and inspiring way to those whom we are in a position to influence.

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If health education is to develop as it should, it must have the right set-up and machinery. This is a field where voluntary or quasi-official organizations can do better work than Government Departments. The war has shown that people are

suspicious of official advice on health. They fear that it may not be disinterested, that it is an attempt to force upon them something that the Government desires them to accept for reasons other than those purely concerned with their individual well-being. Health education, too, should be free from political bias or pressure, and to be effective must always be a little—although not too much—in advance of public opinion. For all these reasons the proper line of development is for the Government to entrust health education to some such body as the Central Council for Health Education, which is the existing agent of the Government and the Local Authorities in England and Wales.

If health education is to be carried out along scientific lines, the needs and the results must be constantly assessed. This has already been done in a number of instances by the War-Time Social Survey of the Ministry of Information, and valuable information has been gained. There is a real need, however, for a systematic assessment of public opinion on matters affecting health, and for a study of existing health habits. Upon this study we can base our health education programme. And, finally, we must measure the relative efficacy of different media and the result of all our work by assessing the changes that have been brought about in health habits, attitudes and opinions.

Dr. N. M. Goodman said that considerable attention had been paid by the Health Division of UNRRA to the possibility of assisting popular health education in the countries in Europe in which UNRRA was operating. He had reluctantly come to the conclusion that health propaganda could not be exported and must be based on local conditions and originated in the country concerned. He also drew attention to the lack of co-ordination in this country in the teaching of preventive medicine, including health education, to medical undergraduates.

Dr. Robert Sutherland said that health education was a problem in education and not in propaganda: it must be something that coloured the whole life of the individual. It followed that it was best carried out by people who in the course of their day-to-day work were in a position to influence for better or for worse the attitudes, habits and knowledge of others. Amongst these, the parent was, of course, outstanding, and he would like to add the parent to Dr. Hill's group of doctor, teacher and health visitor. The Central Council for Health Education attached great importance to this health education of the natural health educators and, at the request of local authorities, was giving courses in the content and methods of health education throughout the country to such groups, and to midwives, district nurses, school nurses, industrial nurses, and industrial welfare workers.

Nevertheless, although the leaflet, the poster and the press advertisement were less effective than this personal health education, they were of some value, particularly in support. Leaflets, for example, were most effective if they were distributed following a lecture or to support advice given individually by a doctor or a nurse. The best results would be got from health education if there were a carefully integrated use of all media. They all had their time and place and had more effect used jointly than severally. Health education along those continuous and planned lines could undoubtedly make a real contribution to the improvement of individual and community health.

Section of Urology

President—A. WILFRID ADAMS, M.S.

[January 31, 1946]

Retropubic Prostatectomy

By TERENCE MILLIN, F.R.C.S.

RETROPUBIC prostatectomy, albeit a British product, is, I believe, the most universally applicable operation yet devised to eliminate the evils of the obstructing prostate. It has its faults, no doubt. What operation in the whole realm of surgery has not? After an experience now of some 85 cases, I am more than ever convinced that it gives me better results than any other I have tried, for every type of case, excluding the fibroses, where, I believe, endoscopic resection reigns supreme.

Before abandoning operations which, you may say, have served us well in the past, we must be reasonably satisfied that the new is better. It is agreed that far too many cases come to us too late, but until we can offer the prostatic patient an easy and relatively safe cure for his troubles, he will not come early, nor indeed are we justified in advising early operation. The present state of affairs is a vicious circle.

In assessing the results of any operation one has to consider mortality, the post-operative course—not only from the surgeon's view-point, but also the patient's—and finally the long-term result.

Mortality.—As far as I know no one in this country has yet published his mortality figures for the Harris operation over an extended series of cases. Through the courtesy of the Staff of St. Peter's Hospital, where most accurate records are kept, I am at liberty to state that the mortality rate for the modified Harris operation during the years 1938-39 was rather more than 10%. These would appear to compare unfavourably with Harris's Australian figures, but there seems to be little doubt that the cases met with here are poorer surgical material than those in the Dominion, and I have it from other Australian surgeons that they cannot approximate to Harris's published results. Mortality figures depend so much on the surgeon's selection of cases.

In the two-stage Freyer technique considerably more die from the preliminary cystostomy than from the subsequent prostatectomy. Cystostomy, simple operation though it be, carries a very appreciable mortality, figures ranging from 4 to 20% if considered over a large enough series to be statistically significant. Again to quote St. Peter's Hospital figures, out of 53 cystostomies, carried out in cases of prostatic obstruction during the years 1938-39, 10 died—a mortality rate of 19%. The second-stage procedure averages out with a mortality rate of 4% in the best hands. It must also be reckoned that a number are left to lead a miserable existence wearing a suprapubic tube, deemed unfit to stand

the rigours of a prostatectomy. The mortality rate of the two-stage Freyer technique is about 8%. In the transurethral techniques, when competence has been acquired (and this is a lengthy process) the immediate mortality should be lower. In my last 200 cases I lost 8. I have had better series, but all in all the death-rate has been about 4%.

Barrington published the St. Peter's figures for prostatic surgery for the five years 1934-38, and reported in 582 cases a mortality rate of 9.07%. Cabot from the Mayo Clinic reported a death-rate of 9.51% in 600 open operations for prostatic obstruction. Here is a table showing my own results where a selection of methods was employed. It is, of course, also a more recent series, where ancillary aids such as sulphur drugs, blood banks, &c., were available.

357 CASES OF PROSTATIC OBSTRUCTION.

Type	Number	% of total	Deaths	Mortality rate
Harris	63	18%	3	4.8%
Freyer (including cystostomy) ...	73	21%	6	8.2%
Endoscopic resection... ..	219	61%	9	4.1%
Radical perineal	2	—	0	—

Total mortality rate for 357 consecutive cases, 5.0%

Post-operative course.—The possible complications of the Freyer technique are well known. This 45-year-old operation fulfils few of the canons of modern surgical technique. The post-operative course is very uncomfortable, and by no means short.

The post-operative course of the Harris case is in general much easier than that of the Freyer, provided that the hæmorrhage has been controlled on the table, and that frequent disturbing wash-outs are not required to maintain free catheter drainage. The same remarks apply to the resection case. I learn that it is common in the clinics of those utilizing the cold punch technique for the unfortunate patient to be disturbed every few minutes for bladder lavage. My own practice when employing the Harris technique was to use a suprapubic catheter for two to four days with continuous irrigation. In resections I use the loop technique in preference to the punch, control the bleeding reasonably well on the table, and then rely on a No. 24F gum-elastic catheter for forty-eight hours to take care of the post-operative oozing. Again bladder lavage is the exception. The post-operative course of the retropubic case is incomparably easier than any of the other open operations.

Late results.—The end-results of the Freyer are on the whole excellent, but shelf formation does occur in a proportion of cases. Even the excision or punching out of the posterior lip of the bladder neck does not guard against this.

The Harris operation carries its own particular late complications. I have already mentioned in a communication to this Section the truly dreadful post-operative obstruction one meets with occasionally after Harris suturing in which the whole prostatic urethra is strictured. There is also a quota of meatal and other urethral strictures when a relatively large catheter has been employed for ten to fourteen days. Another complication, seldom mentioned, which I find occurs not only in my own cases but in those of other surgeons, is a degree of incontinence lasting for a variable number of weeks. These usually clear up, but I have had to deal with two cases of persistent incontinence from other clinics.

Of the late results of the transurethral resections I must speak at greater length. These operations, loop or punch, have proved of inestimable value in dealing with many types of prostatic obstruction, especially the fibroses. They appeal to the public in that no external cutting is involved, and the hospital stay is short. I can claim, I think, a wider experience of these operations than anyone in this country. I have long been an ardent advocate of their use in the lesser obstructions, the poor risk case, &c., but with a full realization that they had their limitations, or rather should have. The transurethral resection cannot be a complete adenectomy despite claims to the contrary. The bogies of recurrent obstruction and persistent infection are ever present. I have a number of patients now resected more than ten years ago, who have had no further trouble, but other cases have not been so fortunate. I have always admitted this, but felt that in many cases the alternative was unduly hazardous, and that it was better to be alive with the risk of recurrent obstruction than dead, cured. To my mind, the greatest bugbear of resection is the risk of subsequent urethral stricture. Early in my urological career I learned that it was unsafe to pass an unduly large instrument along the male urethra. The commonly used Thompson Punch, euphemistically calibrated 30F, is doing irreparable damage. I have recently had 3 members of one London club, resected in the same clinic, all with the most appallingly strictured urethræ. Two of them, by the way, had

two resections at approximately three months' interval, indicating that the complete prostatectomy claimed by the ardent advocates is evidently not so complete. All these men face the picture of monthly bougies for the rest of their lives. One has also recurrent prostatic obstruction. These represent therapeutic disasters. I personally never exceed a No. 28F instrument, and in a number of cases even this cannot be safely passed, a perineal urethrostomy being necessary. Reed Nesbit, one of America's leading resectionists, is, I understand, now employing a urethrostomy in 25% of his cases.

Of the sequelæ of the perineal operation I shall not say much. It has never had a great following in this country, and even in America its advocates are dwindling. You all know the ghastly messes which can occur even in the best hands. I have recently had a pitiful letter from a patient who was subjected to a perineal prostatectomy at the age of 37. Now, fourteen months later, he is still in hospital with a leaking suprapubic fistula, a colostomy, a urethrorectal fistula, and a perineal sinus. There appears to be a slight tendency to return to the perineal route in some quarters quite recently, no doubt due to a dissatisfaction with the accepted suprapubic procedures, and a glib acceptance of certain published figures which scarcely convey the whole truth.

That the enucleation of a simple tumour should entail such hazardous adventures appeared to me to be a blot on modern surgical achievement. I for one had a sense of frustration; I sought elsewhere. The subpubic operation mentioned by Uteau and Leroy proved impracticable. Noting the excellent exposure of the prostate during the operation of cystectomy, I turned to the retropubic approach. From the very first I have been pleased with this. It is virtually a perineal type of prostatectomy performed well away from the rectum and compressor urethræ—the twin bogies of the inferior approach. Moreover, the nerves and arteries of chief moment are situated posteriorly, the anterior aspect of the prostate being accessible without damaging structures other than veins. Anteriorly also the urethra is closest to the surface of the gland, and the ejaculatory ducts are less liable to damage than in the perineal operation. It does not seem to be sufficiently appreciated that the level of the internal meatus is approximately the upper limit of the pubis in the vertical position, and is even higher when there is marked prostatic enlargement and elongation of the prostatic urethra. The retropubic exposure is thus not via a dark, deep, and dangerous hole, as has been suggested by some. The normal anatomy of the approach presents no structures of importance which need be sacrificed. Venous bleeding during the sectioning of the prostatic capsule can be troublesome if adequate care is not taken to deal with these veins, either by ligature or appropriate clamp before division. With the technique I use to-day this bleeding is usually negligible. Three arterial anomalies may be met with, and should be known. I am indebted to my assistant, Mr. Ashton Miller, F.R.C.S., for researches into this subject.

(a) *Accessory pudendal artery*.—This is a sizable vessel which may be met with on the lateral surface of the prostate. According to Buchanan it is only present occasionally, and arises from the intrapelvic portion of the internal pudendal, or from the inferior vesical artery. It passes forward along the lateral aspect of the bladder and prostate to the triangular ligament, which it pierces, branching into deep and dorsal arteries of the penis, and, rarely, the artery of the bulb.

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These vessels might be injured either during the initial sectioning of the prostatic capsule, or later during the suturing process.

(c) *Aberrant obturator artery*.—This is a better-known anomaly, occurring, according to Gray, in 28% of subjects. It replaces the normal artery, and arises from the deep epigastric of the same side near its origin, passing behind the lacunar ligament, and downwards to the obturator canal. It does not itself lie close to the scene of operation, but the vesical branch normally arising from the obturator artery in the pelvis may spring from this anomalous vessel, and pass via the pubo-prostatic ligament and antero-lateral aspect of the prostate to the bladder.

Now as to the so-called internal sphincter. The classical transvesical procedure entails the division of this structure first with the finger, and later during the delivery of the lateral lobes into the bladder. It is well known that stretching any sphincter entails shock. Moreover, post-operative urethrograms show that in a large proportion of cases the bladder neck remains patulous, and the patient is entirely dependent on the compressor urethræ for continence. Some go a stage further, and fearing a shelf formation due to fibrosis following sepsis, excise or punch out a wedge of trigone, a completely unphysiological

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procédure. Some Harris advocates, on the other hand, actually attempt to narrow the bladder outlet, and draw down the trigone into the prostatic bed, so bringing the ureteric orifices almost on to the bladder neck, as seen at subsequent cysto-urethroscopy. In one operation the bladder neck is deliberately enlarged, in the other it is equally deliberately narrowed. Why not leave it alone? This is what one does in the retropubic operation. I must qualify this statement, as when after enucleation of the adenoma one finds the bladder neck sclerotic on palpation, a wedge excision of the neck should be made.

I have repeatedly shown by means of a finger in the bladder where the retropubic procedure has been carried out after a preliminary cystostomy, that the bladder neck is relatively little disturbed even where a large middle lobe, or other intravesical projection, has been removed from below. This is confirmed during one-stage operations, when it is noted that after enucleation there is no escape of urine through the sphincter, yet the stretching of the structure to allow the catheter to pass leads to an escape.

One other point, perhaps of minor importance, is the sexual aspect. It is well known that after the classical prostatectomy, when potency is retained, there is little or no external flow of seminal fluid on ejaculation, apparently owing to lack of competence of the internal sphincter. I have records of two of my retropubic prostatectomies who do ejaculate a reasonable external discharge. In the past I have had several patients who have expressed extreme displeasure at the phenomena observed after a Freyer prostatectomy.

To sum up these considerations, it would appear that the retropubic operation is anatomically the logical one, and that best calculated to remove the obstruction completely, with the least damage to important structures.

Let us consider now the practical aspect, taking in turn the pre-operative care, the actual operative technique, and the after-care. We shall later review results, comparing those obtained by other methods.

In considering pre-operative care I am not unmindful that there is no unanimity as to handling of the various types of case met with. I shall give briefly my own practice:

(a) Case with marked prostatic symptoms, uninfected urine, no great clinical residuum as evidenced by palpation or percussion, and an enlarged gland on rectal examination: In most of these cases I do not trouble my pathologist with extensive renal function tests, but rely on clinical assessment, blood-urea estimation, and, when possible, intravenous urography. If operation is decided upon, renal function being good and other demonstrable pathology being absent, no urethral instrumentation is employed until the patient is on the operating table, when cysto-urethroscopy is carried out. Decision is then made as to whether resection or prostatectomy is the order of the day, and the appropriate measures performed there and then.

(b) Case of acute retention: Where condition is good and early operation is indicated, suprapubic tapping is sometimes employed for a day or two. In most cases a urethral catheter is used, always combined with sulpha drug therapy and forced fluids. Where urinary excretion, renal function tests, or cardiovascular system are inadequate, the decision is made as to whether to continue with urethral catheter drainage, or to carry out a high cystostomy. In most cases met with in this series catheter drainage has been adequate.

(c) Chronic retention: Here the choice will again lie between urethral catheter and cystostomy. I personally usually rely initially on slow decompression via a catheter for the first twelve to twenty-four hours; later spigoting the catheter and releasing it two-hourly. This I regard as more physiological than keeping the bladder constantly empty. Unless the catheter is not tolerated, I rely on this for seven to ten days, and if the renal function is then not reasonably good, perform a cystostomy. I find, as did Harris, that it is only the exceptional case which does not respond to catheter drainage, but I do not hesitate to carry out cystostomy where indicated.

(d) Cases of gross urinary infection and very poor renal function will almost invariably call for cystostomy: Where the function tests are reasonable, sulphonamides and the urethral catheter will often work wonders with sepsis, and render a one-stage retropubic prostatectomy a safe procedure.

These brief rules are, of course, only approximate, as there are always the exceptions.

Associated urological pathology.—I shall only mention those pathological factors which seem to me to have most bearing on the choice of operation to be advised for the enlarged prostate.

(a) *Vesical calculus.*—Where the stone is a large one associated with much urinary infection, then it should be removed suprapubically and the bladder drained, as I have already mentioned under the heading of gross urosepsis, until the condition, general and

local, warrants a prostatectomy. This may be performed either by the classical Freyer technique, or, as I prefer, by the retropubic route. In the rare case, in which a large stone is found associated with little infection, this may be removed at the time of the retropubic operation, the anterior wall of the bladder being deliberately incised, and subsequently closed in two layers. Where the calculus is smaller, it can be removed by introducing appropriate forceps through the internal sphincter after the enucleation of the prostate. Where the calculus is found in the presence of bladder-neck sclerosis, litholapaxy is carried out at the same time as the endoscopic resection.

(b) *Vesical diverticulum*.—Where a pouch of significant size is associated with prostatic enlargement warranting operation, it has been usually held that the removal of the diverticulum should be carried out as a primary measure, and that after an appropriate period of suprapubic bladder drainage, the prostate dealt with. If a classical transvesical prostatectomy is performed in the presence of a diverticulum there is very great likelihood of a failure of the fistula to close, and the removal of a diverticulum after a previous prostatectomy, where there is a persistent fistula, is a procedure taxing the skill of the most expert. I see no reason why a retropubic prostatectomy carried out in the presence of a diverticulum should not be completely successful. There is no bladder fistula to be persistent, and the minimal amount of bladder infection compared with that in a Freyer would be unlikely to be of serious moment. I have quite recently had the opportunity of performing a retropubic prostatectomy in the presence of a diverticulum, but the case is too recent to report. I do not advocate leaving all such diverticula alone, but there are certainly some of these pouches burrowing deep down under the bladder base whose removal is singularly difficult, and which I feel would be better left alone, merely carrying out a retropubic enucleation of the obstructing gland. The Mayo Clinic workers claim that it is seldom necessary to operate upon vesical diverticula where the removal of the bladder-neck obstruction is effected via the transurethral route. This is a view which has not been universally accepted, but I feel that cases will certainly arise from time to time where the surgeon would feel happier to leave the pouch undisturbed provided he can secure a satisfactory prostatectomy.

(c) *Papillary tumours*.—Each case exhibiting the combination of prostatic obstruction and a papillary growth must be judged on its merits. In general, where the tumour is likely to respond to cystoscopic diathermy, this treatment should be carried out first, using a large electrode through an operating cystoscope. Where it appears necessary to open the bladder to deal with the growth, this should be done as a preliminary measure, and later the gland removed retropubically. Where total cystectomy appears indicated, the problem does not arise.

(d) *Calculus prostatitis*.—The calculous prostate causing marked obstruction, especially when associated with gross infection and impaired renal function, has always been a problem to accepted methods. A one-stage operation is unduly hazardous, and the classical removal as a secondary procedure is not easy. A two-stage retropubic prostatectomy would seem to be the answer to the problem.

Anæsthesia.—Almost any preferred form of anæsthesia may be employed. My preference is for pentothal induction, followed by gas-oxygen or cyclopropane, supplemented by pentothal as required, but never exceeding 1 gramme of the barbiturate. In poor risk cases I utilize an abdominal block, subcapsular infiltration of the prostate, and a very brief cyclopropane or pentothal anæsthesia during the enucleation. A good alternative is caudal plus abdominal block. I dislike spinal analgesia because of its not infrequent unpleasant sequelæ.

Technique.—I have already described fully the steps of the operation,¹ and in the light of subsequent experience have not materially altered the technique. No doubt it can be improved. For the preliminary endoscopic inspection I know no instrument superior to my wide angle vision cysto-urethroscope. It enables us to make a rapid inspection of the bladder for associated pathology, and then assess the intravesical and intra-urethral configuration of the obstruction. Continuous irrigation is, of course, employed. The bladder is emptied, and the endoscope withdrawn. Whilst the operator is changing his gown and gloves the assistant prepares the field, and towels up the patient. Only a short mid-line incision is necessary. The transverse incision which I, like many others, prefer in the Harris operation, has no advantage here. In most of my early cases I employed a standard Harris type of self-retaining retractor. A modification with a movable upper blade is useful. The Harris frame, although apparently cumbersome, has many advantages; it does not tilt, and there are few structures on which catgut, &c., will catch. My modification of the Legueu retractor has the merit of being more rapidly

¹*Lancet*, 1945 (ii), 693.

introduced and removed; it is frequently possible to enucleate the adenoma without removing the retractor, and the flexible upper blade can be depressed by digital pressure.

After exposing the gland I pack 18 in. of 6-in. gauze roll into each lateral recess, i.e. between the lateral aspect of the prostate and the levatores ani. 10 c.c. of 1% procaine, to which 3 minims of adrenaline 1/1000 have been added, are now injected into the gland subcapsularly. This opens up a plane of cleavage, and, I think, helps to minimize bleeding. The three under-running sutures to control the veins are now placed, the ends of the sutures left long, and held with hæmostats. I then make a very short vertical nick through the fascia and true capsule, and insert special L-shaped capsule forceps, one on each side, to clamp any veins not controlled by the stay sutures. A transverse incision is then made, either with a scalpel or the diathermy knife, proximal to the clamps. A T-shaped clamp is then applied to the edge of the proximal flap, controlling the small artery which is usually severed in the mid-line. Three stay sutures are now applied to the proximal flap, one in the mid-line and one at each extremity. The clamps are removed, and any individual veins still bleeding seized with hæmostats and coagulated. The false capsule is then opened with a deep inverted V incision.

This is stripped back off the adenoma, which is also cleared distally and laterally with Devine's chisel-pointed scissors curved on the flat. The urethra is deliberately cut across distal to the lateral lobes, and the latter then enucleated with the right index finger from below upwards. A second finger at this stage of turning the lobes upwards is often useful. It is very rarely necessary to utilize a finger in the rectum. Mechanically the enucleation is far sounder than in the transvesical techniques in that the finger is working at right angles to the urethra, and not in the long axis of a cone. There is no danger of avulsing a strip of membranous urethra. When the lobes have been freed distally and laterally they are delivered into the wound, and held either with the fingers of the left hand or by means of Duval's forceps. The trigone is sponged off the adenomatous mass posteriorly, and the bladder neck off it anteriorly, leaving it free except for a cone of mucosa. This latter is then deliberately cut across distal to the bladder neck. A small pack is now placed in the prostatic cavity, whilst the edges of the false capsule are picked up with Kocher, Allis, or other appropriate forceps. The pack is removed, and whilst the special model sucker nozzle is applied to the prostatic cavity, bleeding vessels are visualized and caught with hæmostats. These are then touched with the diathermy needle. The bladder neck is palpated, and, if sclerotic, a wedge resection is made. A suitable-sized Harris catheter is then passed along the urethra; it is seen entering the prostatic bed. Whilst the assistant opens the internal meatus with the spreader, the catheter is guided into the bladder either with forceps, or with a stilet. The false capsule is then closed with a running suture, utilizing the boomerang needle. Bleeding should now have ceased. The stay sutures are now tied together, mid-line to mid-line, right to right, and left to left, after the upper blade of the retractor has been loosened or removed. The retropubic space is dusted with sulphanilamide powder, and the wound closed routinely with a small corrugated drain down to the suture line. Where the venous ooze has not been adequately controlled, a cigarette drain of gauze is preferred to the rubber drain. (I have had recourse to this three times.) After bilateral vasectomy, the catheter is syringed out with flavine 1/6000, the eyes being suitably adjusted so as to be just within the bladder. The catheter is fixed with silkworm gut sutures to the penis. The whole operation need not exceed half an hour, and is frequently completed in under twenty minutes. 4 oz. of 3.8% sodium citrate solution is left in the bladder, and the catheter spigoted. One hour after the patient returns to bed the spigot is released to verify that the catheter is draining, which being so, it is again spigoted. One hour later the spigot is removed, and the catheter connected via sterile tubing to a Winchester at the side of the bed. Aperients are administered on the second evening, and on the third day the patient is allowed up to use the commode. From the fourth day onwards he gets up to sit in the chair. During the day the catheter is spigoted, and released two-hourly. I repeat that I regard this intermittent filling of the bladder as more physiological than keeping the viscus constantly empty. Only in 1 case in 8 is post-operative syringing of the catheter necessary. The drain is shortened on the second day, and removed, in general, on the third day. The catheter is removed on the fourth or fifth day, unless the procedure has been carried out after a preliminary cystostomy, in which case it is left in ten days. Some suprapubic leakage will occur in a small proportion of cases. It is neglected for twenty-four hours, and, if necessary, a small catheter is replaced until the wound is sound and dry. Where a chronic retention has been present before operation the atonicity of the bladder may lead to a retention; if it does not respond to a parasympathetic stimulant further catheter drainage may be necessary. Twice I have seen a retention follow the removal of the catheter due to spasm in nervous patients; a hypodermic of morphia will relieve this. A sulphur drug is administered routinely for

forty-eight hours before operation, and for five days subsequently, unless contra-indicated. The minimal amount of post-operative infection of the urine is noteworthy, and the rapidity with which the urine becomes clear is in marked contrast with that found after the Freyer technique. All patients report two to three weeks after dismissal from hospital, and it is quite exceptional not to find clear, or only faintly hazy, urine on this visit. Instrumentation is employed only where the urinary stream does not appear adequate.

I have employed both thrombin topical and fibrin foam in the prostatic cavity, but cannot claim that they proved any help, nor indeed are they necessary.

Post-operative Complications

These have been in the main singularly infrequent. The comments of the nursing staff, who have also to deal with prostatectomies handled by the older methods are flattering, and mirror my own views. It is only the exceptional case which requires time-consuming bladder wash-outs; even bedpans are unnecessary.

Reactionary hæmorrhage.—I have as yet met with no case where anything more than a bladder lavage has been necessary.

Secondary hæmorrhage.—This I have had four times. All responded to lavage through a catheter, though in one case a fatal pyelonephritis followed. Suprapubic cystotomy for such a complication has in no instance been necessary.

Pyelonephritis.—2 cases have been met with. In one the patient had just recovered from an attack of pyelonephritis associated with retention due to a very large gland. Prolonged catheter drainage had been employed elsewhere. The patient, a doctor, was very averse to a cystostomy which I recommended, and against my better judgment I performed a one-stage retropubic prostatectomy. The immediate post-operative course was completely uneventful. The catheter was removed on the sixth day, and easy voiding followed. On the tenth day pyrexia set in, which failed to respond to sulphanilamides, penicillin, &c., and he succumbed to a recurrence of his pyelonephritis. He was 76, and an admittedly poor risk. In the other case I have no excuse to offer. He was an apparently fit man of 55. The enucleation was not easy, as a subtrigonal nodule had to be dissected from the bed, in addition to large lateral lobes. Secondary hæmorrhage occurred on the sixth day, as mentioned earlier, which responded to bladder lavage, but a pyelonephritis developed later, and he succumbed on the eighteenth post-operative day.

Post-operative urinary leakage.—This will occur in a small number of cases. I feel that, provided the closure of the cavity has been satisfactory, this is due to too early absorption of the catgut. In one case this was clearly demonstrated. The catheter slipped out twenty-four hours after operation, and the house surgeon was unable to attend to the patient for some three hours. During this time urine was voided easily twice, and without leakage. The catheter was replaced, but on its removal on the sixth day, urine escaped from the wound. I now employ No. 1 chromicized catgut for the capsular repair. Every effort must be made to secure a watertight closure of the prostatic cavity; it makes for easy post-operative course, and early dismissal.

Post-operative stricture.—It is obviously too early to comment on this. In 3 cases seen at the first check-up after dismissal the urinary stream was not full, and steels were passed. In all there was some gripping at the bladder neck. A timely dilatation at this stage of soft infiltration will save trouble later.

Pulmonary embolus.—I have as yet met with no case. I attribute this largely to the short period of confinement to bed.

Femoral thrombosis.—The only case I have had was the first in the series already reported, where gross urinary infection preceded the operation due to three years' self-catheterization.

Post-operative fistula.—Despite the armchair fears of some on this score, this has not occurred, nor do I see why it should.

Incontinence.—No case of even temporary incontinence, partial or complete, has been met with. The preservation of both sphincters should render such a possibility very remote.

Clot retention.—I am informed that the armchair detractors of the retropubic procedure hold this as a dread and likely complication. Let me answer them here and now that I have not met it in a form not easily handled through the catheter. I admit that it remains a real possibility, as after any prostatic operation yet described. Should this occur, and the bladder be already opened, the situation is more easily taken care of, but dealing with such an occurrence after a retropubic operation should not be outside

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(f) *Sexual sequelæ*.—In no other operation with which I am acquainted is the phenomenon of external ejaculation noted afterwards, excluding, of course, minimal resections.

Here are the facts and figures of my experience with this operation. Including every case of prostatic obstruction admitted to my wards and private beds during the period since August 26, 1945, when I performed my first retropubic prostatectomy, I have dismissed 1 case wearing a suprapubic tube (blood urea over 200 despite prolonged drainage), have performed 1 Freyer enucleation (in private, early in the series). 1 patient was admitted moribund with retention and advanced uræmia, and succumbed six hours later without my ever having seen him. Another case, admitted with severe spontaneous prostatic hæmorrhage and clot retention, was subjected to cystostomy. The following table will indicate the procedures carried out in the remainder:

One-stage retropubic prostatectomy	74 cases
Two-stage retropubic prostatectomy	{ cystostomy elsewhere	7 cases
	{ cystostomy by me	3 cases
Endoscopic resection	4 cases
Retropubic evacuation of prostatic abscess	1 case
Suprapubic cystostomy (awaiting second stage)	2 cases

In conclusion, I commend with every confidence this operation as a sound rational procedure, the practical results of which bear out the obvious theoretical advantages. It may be carried out either as a one-stage procedure, or after preliminary cystostomy, and in my view it is the procedure of choice in every case affording a reasonable operative risk, excluding the fibroses, where endoscopic resection holds the field.

Many of you have, I know, performed the operation, and I look forward to hearing of your experiences, and, no less, the criticisms of others still faithful to the older methods.

The President: In opening this discussion my chief duty, and a very pleasant one, is to say how privileged I feel to be here to-night and how grateful we are to Mr. Millin for his admirable review of prostatectomy up to date and lucid description of this new addition.

In prostatic hypertrophy the genital pedestal swells and strangulates the urethral exit beneath the urinary chamber. Mr. Millin makes a direct attack on the obstacle and saves adding surgical injury to a bladder which has long suffered pathological insult. This struck me as a bold strategic move in prostatectomy when first he shared his new retropubic operation with the Royal Society of Medicine last November. The intact bladder is ready for action when the artificial drainage is removed. The post-operative course is correspondingly easier than that following the transvesical route, but has its complications. The packing of fat in the spaces round the bladder neck is favourable soil for sepsis and has for long made the cave of Retzius a place of evil repute. Throwing tradition aside, however, Mr. Millin elects to approach the prostate through it. Has the region been malignised? Parietal sepsis has certainly been the rule rather than the exception in my 8 cases, though the discharge of pus has been but transient. The resumption of natural micturition following withdrawal of the catheter whether early, fourth day, or as late as the tenth post-operative day has in several proved a time of distress and anxiety. The patient appears liable to spasm like a veritable vesical crisis which in 1 case needed suprapubic puncture for its relief. Considerable negotiation may be needed to coax the tip of sound or catheter into the bladder.

But the risk of a more subtle form of post-operative obstruction attends this operation and led to the second of the two fatalities among my series. An elder of 79 years and a chronic bronchitic, died suddenly of pulmonary embolism when healed and ready for home. In the second fatality, the patient had trouble after removal of the catheter on the eighth post-operative day. The house surgeon reinserted the catheter. It did not function well, there was increasing uræmia and urinary output was fitful and finally appeared to cease. Post-mortem revealed a stagnant bladder with about 12 oz. of purulent urine pent up by a pair of apposed vesical "tonsils" overlying the outlet of the bladder and consisting of adenomatous prostatic remains! These fatal relics of the prostate were evidently growing semi-detached from the main subvesical mass and it was easy for such to escape the sweep of the enucleating finger. The moral is to palpate the lining of the prostatic cavity for buried nodules and pass the finger round inside the bladder neck in doubtful cases.

One of the advantages of such total enucleative operations as Mr. Millin's over the resecto-punch method of prostatectomy lies in the completeness of removal and consequent good hope of cure in cases of "enclosed" cancer unsuspected before or during operation.

Mr. R. Ogier Ward stressed the fact that the operation should not be described as an easy one. Once the surgeon was committed to it he must continue and complete it. It was not possible to stop and be content with bladder drainage.

Mr. E. W. Riches: A discussion of the results of the new operation would be premature at this stage. There are two sound principles involved in its performance, a direct approach to the site of disease, and enucleation of the prostate from below starting at the lower borders of the lateral lobes. This latter principle has also been stressed by Harris and prevents the removal of a tube of urethral mucous membrane below the verumontanum which is one of the causes of post-operative stricture. Regarding details it is unfortunate that a very vascular area has to be traversed; if the incision in the false capsule is made

the scope of any surgeon embarking on this form of surgery. Few clot retentions fail to respond to the aspiration technique, provided a suitable catheter and syringe are to hand. If this should fail, it would only be necessary to remove the uppermost two sutures in skin and aponeurosis, plunge a knife into the bladder, evacuate the clots with a sponge forceps, and leave in a suitable drainage tube. This procedure could be performed without even removing the patient from his bed. If the situation should arise after the wound is healed, anaesthesia might be required to reopen the uppermost part of the wound. I repeat I have not experienced it in over 80 cases.

Mortality.—Amongst these 85 cases I have had 4 deaths—2 from pyelonephritis already mentioned, and 2 from cardiac failure within forty-eight hours of operation. In 2 of these 4, I operated against my better judgment, each refusing a preliminary cystostomy. Representing as this does a continuous series, and an initial one at that, I am confident that even better figures will be forthcoming. The first death incidentally was in the thirty-first case. This is admittedly too small a number from which to quote mortality rate. For what it is worth, it represents under 5%.

Operative Difficulties

Anatomical anomalies.—These have already been described, and could conceivably prove troublesome if the operator were not aware of their presence, and on the look-out. I have met with only one abnormal artery—a deep penile branch from the obturator. It was clearly seen when the prostate was exposed, and was doubly clamped, cut, and diathermized.

In one case, a very large irreducible scrotal hernia made exposure of the prostate on that side none too easy, but the enucleation of a 127 grammes gland was effected successfully.

In another case, the removal of a very adherent fibro-adenomatous gland, associated with a thin-walled bladder, led to a tearing of the anterior fibres of the sphincter. These were sutured.

Second-stage prostatectomy.—I have found no particular difficulty in carrying this out, and I regard it as preferable to a Freyer enucleation where a previous cystostomy has been performed, even in cases where the fistula has been established adjacent to the pubis. Where the opening is low, I make a transverse incision, partially dividing the tendons of the recti; otherwise, a vertical mid-line incision downwards from the fistula. The adherence is merely at the muscle level, and the retropubic space opens up readily to expose the prostate. The enucleation and suturing of the capsule are routine. The bladder fistula is then closed. No extensive dissection of the track is necessary. The mucous membrane is freed and inverted with a pursestring. The aponeurosis is approximated superficially, and the skin closed. The whole procedure need not take more than thirty minutes. My reason for performing a retropubic prostatectomy as a secondary procedure in preference to the more expeditiously carried out Freyer enucleation is that I believe it is more benign—there is less shock, less post-operative bleeding, less post-operative discomfort, less risk of persistent fistula, and a more speedy dismissal from hospital. I believe that the extra ten to fifteen minutes on the operating table are well spent.

Finally, let us compare the retropubic operation with other accepted techniques.

(a) *Technically* the operation is far easier to master than either the perineal or transurethral. It is no more difficult than the Harris, and though admittedly not an operation for the occasional prostatectomist, as is the Freyer, should be well within the scope of the trained general surgeon.

(b) *Mortality.*—Preliminary experiences indicate that the risk should be less in this operation than in any other, excluding perhaps the transurethral. The demerits of the latter in the grosser hypertrophies have already been indicated.

(c) *Post-operative course.*—This appears to be easier for both patient and surgeon than in any rival procedure. Indeed, one of the most striking features of the operation is the almost complete freedom from pain. The spasms common in the Freyer operation are not seen.

(d) *Hospitalization.*—This is in general far shorter than in any other open operation.

(e) *Long-term result.*—It is too early to comment on this, but I see no reason to believe that the results should be inferior to those obtained by any transvesical approach. They are without doubt better than those obtained perineally, and by virtue of the completeness of the operation, should certainly transcend the transurethral.

In the other case, there were five medium-sized stones in the bladder. It had been my intention to deal with these through a separate incision in the bladder wall. I found, however, that it was easy to feel the stones on passing a finger through the internal meatus and so I extracted them through this route, thereby, I think, unduly stretching the bladder neck. Urinary leakage occurred on the fourth day and this soon became obviously infected. Twelve days after the operation, an abscess appeared over the gluteal region, which had to be evacuated.

These incidents do not detract from the merits of the operation, but rather serve to emphasize the necessity of adhering to the technique described by Mr. Millin. It is of importance to make certain that the catheter has been properly inserted into the bladder and that it does not become displaced whilst completing the operation.

The operation is perhaps technically more difficult than the suprapubic method, but can, nevertheless, be expeditiously accomplished. When the operation is completed, the after-treatment is simple and no specially trained team is required to carry it out.

Mr. Clifford Morson (*in absentia*, read by Mr. Ainsworth-Davis): There seem now to be almost as many techniques for prostatectomy as there are urologists in this country. The explanation is simple. Surgeons are dissatisfied with many of the end-results, and it is not to be wondered at when it is remembered how much damage is done to the urethra by the removal of the prostate. Surgery can never be the last word in the treatment of this disease. It is dangerous to dogmatize about the results of a new operation until it has had a fair trial, but I certainly like the simplicity and minimum of damage to surrounding tissues of Mr. Millin's technique. However, I cannot give whole-hearted support to it until I know what are going to be its remote results, and for this we must wait two years. In a ward of one of my hospitals there lie side by side suprapubic and retropubic cases. The only difference in the post-operative convalescence is the anxiety about the tied-in catheter blocking with a closed bladder. As for length of stay in hospital both are healed in about a fortnight, but he is a foolish surgeon who hurries his prostate cases out of hospital. I would remind you of the investigations of Semple and myself some years ago which showed that the rate of healing in the prostatic cavity was extremely slow, and many weeks after the abdominal wound had healed there was a raw surface. The extent of that raw area is reduced by a plastic operation such as Wildbolz's or Harris'. Now that is what affects the remote results. The more scar tissue there is uniting bladder mucous membrane to urethral mucous membrane the more urinary dysfunction there will be. Scar tissue contracts slowly so that the dysfunction may not manifest itself for a long time. I think that like the suprapubic operation, the retropubic will give good immediate results. An amazing change has come over the results of suprapubic prostatectomy in the last five years thanks to the complete control of bladder sepsis. Secondary hæmorrhage now is very rare.

Electrolytic sodium hypochlorite, the sulpha drugs, urea formic iodide, and now penicillin are all playing their part in reducing complications and the mortality rate. Professor Noordenbos of Amsterdam in a recent speech at the College of Surgeons stated that the introduction of penicillin had caused the greatest revolution in surgery since Lister. There is no reason to-day why any prostatectomy case in private practice should die of a urinary complication. In my last 40 cases in private practice I have not had a death. For the past 2 years I have had 60 cases at a municipal hospital with 2 deaths. It is notorious that many of these patients are poor surgical risks and yet they survive the operation. Mr. Irwin at St. Paul's is getting similar results.

Mr. Alex. E. Roche: The main advantages of Mr. Millin's operation are not its low mortality or the short period in bed—about two weeks. Similar advantages are claimed for perurethral resection and for Steinach II, which both have this advantage over Millin's operation, of avoiding a suprapubic incision.

Nor is the absence of suprapubic leakage of urine the main advantage of this operation. That, again, is shared by the perurethral resection and Steinach II, not to mention Harris's prostatectomy with closure.

No, the main advantage, it seems to me, is that, unlike perurethral resection and Steinach II, Millin's operation is radical.

The absence of mortality in 20 cases is good, but, of course, we all have runs of 20 or more prostatectomies without mortality. Personally I like to have, and I think I can achieve, a low mortality in my prostate operations—perhaps 5 to 7%. I do a two-stage Freyer-like prostatectomy—an operation which will, I think, last as long as prostatectomies are being performed.

With regard to nomenclature all suprapubic operations are retropubic when the patient is supine, but, whereas ordinary suprapubic prostatectomy is transvesical, Millin's is prevesical, so I prefer the term prevesical prostatectomy to retropubic prostatectomy.

Mr. John Everidge: I think too much has been said about spasms arising as the direct result of incision through the bladder wall. After all we do not see spasms after simple suprapubic drainage nor after partial cystectomy, &c., in either sex. A further factor must be necessary.

Mr. F. E. Feilden: In my view there is no one approach to the pathological prostate; each case must be considered on its own merits, and the appropriate route selected after careful pre-operative investigation. I do not think the post-operative pain referred

vertical fewer vessels are divided, but even so it is a bloody operation, although there is little bleeding from within the prostatic cavity. I do not like the preputial stitch and prefer to anchor the catheter by a sling stitch passed through the fundus of the bladder to a button on the abdominal wall. The catheter is the weak point of the operation as it is in the original Harris procedure, the danger being urethritis. In eight cases there has been one of œdema of the penis and urethritis, and this patient had a secondary hæmorrhage with clot retention on the ninth day; it was relieved by catheterization and glycerin of pepsin. Cysto-urethroscopy has been done in all my cases between the ninth and the nineteenth post-operative day, and it invariably showed some sloughs in the prostatic urethra or at the bladder neck. I do not think therefore that patients should be discharged in a fortnight, I prefer to keep them in for three weeks.

A urethral catheter for preliminary drainage carries the same danger, but suprapubic catheterization makes a two-stage operation quite possible if the catheter is placed high, and four of my cases have been so treated. I prefer a transverse skin incision.

As compared with the Harris operation the approach is more difficult but the reconstruction easier. There appears to be little difference in the final results but the immediate convalescence is smoother after the retropubic operation owing to the absence of bladder spasms. The future development of the operation lies in the possibility of reducing the period of urethral catheter drainage.

Mr. H. K. Vernon: I have performed the operation on 13 cases, so far without mishap. From this limited experience I am as yet unconvinced that it is the operation of choice as a second stage procedure. One of my difficulties has been oozing from branches of the dorsal vein of the penis due, no doubt, to faulty placing of the ligature and injury of the veins by the boomerang needle. In the last case I decided to perform the operation without preliminary ligature of the vein, but the bleeding after incising the capsule was more than in the other cases. The operation is completed more quickly if the bleeding from the plexus is largely ignored until after the prostate is enucleated. Hæmorrhage is then easily controlled.

Mr. Arthur Jacobs: Since Mr. Millin described his operation, I have performed retropubic prostatectomy on 19 occasions. I well realize that such a limited series carried out in a period of under two months is of no value as a basis for any statistical study, but it has provided me with sufficient experience of the operation to enable me to say that I believe the claims made for it by Mr. Millin are justified. Occasional difficulties and complications, however, do arise.

My patients represented the usual cross-section of prostatic cases with varying degrees of cardiovascular and renal impairment and 3 were in the age-group 70 to 77. Of the 19 cases, I had 1 death, the circumstances of which I shall describe to you shortly. 16 of the patients had an uneventful recovery. Some urinary leakage occurred in 3 of these, which, however, ceased spontaneously in fourteen, sixteen and twenty-one days respectively. All were up on the fourth or fifth day and with the exception of these 3 cases and not counting, of course, those operated on in recent days and still under my care, were able to go home in twelve to sixteen days. One of the patients had a persistently blood-stained urine throughout the period of post-operative catheter drainage and, on removing the catheter, was unable to void urine. On passing a gum-elastic catheter, a collection of small clots was evacuated by suction with a syringe. The catheter was tied in for twenty-four hours and there was no further trouble. That was the only incident of bleeding; it was not serious and was easily dealt with.

The one mortality occurred with my eighth case. The patient was a man of 64, with a retention of ten days' duration, which his doctor had been relieving by catheterization. There was a history of previous cardiac trouble and an increased cardiac dullness with a rough murmur at the aortic area were present. The hæmoglobin was 48% and the R.B.C. just over 3½ millions. His blood urea on admission was 110 mg.% and intravenous urography carried out after a few days' catheter drainage and forced diuresis showed moderate dilatation in the right pelvis and calices and marked dilatation on the left side. After eleven days' catheter drainage, by which time his blood urea had fallen to 56 mg.% and his secondary anæmia had improved with coliron and anahæmin, operation was proceeded with and was easily accomplished within thirty-five minutes. On proceeding to place the retention stitch and irrigate the catheter, it was found that the latter was not in the bladder. It had either become displaced or had not been properly inserted and all efforts to replace it failed. I was finally compelled to pass a metal catheter, which was the only type I could guide into the bladder and tied this in. About twenty minutes were occupied with these manœuvres and, by the end of that time, the patient had become quite markedly shocked. He failed to respond to plasma infusion and other supportive treatment and died seven hours after the operation. I feel that if this trouble with the catheter had not occurred, the patient, though not a good operative risk, would almost certainly have come through successfully.

There were complicating incidents with two other cases. In one, this was again the result of the catheter becoming displaced from the bladder. Profiting from my previous experience, when I found it could not be immediately replaced, I reopened the abdominal wound and inserted a Malecot tube into the bladder. The tube was delivered through the lower extremity of the incision and the wound resutured. It was interesting to observe that although some 6 oz. of flaving had been instilled through the catheter, none of it had permeated through the sutured prostatic capsular layers. On the removal of the suprapubic tube ten days after operation, normal voiding was gradually resumed and the patient left hospital on the twenty-eighth post-operative day. Final closure of the sinus followed the insertion of a catheter, which was passed into the bladder without difficulty and retained for three days.

In the other case, there were five medium-sized stones in the bladder. It had been my intention to deal with these through a separate incision in the bladder wall. I found, however, that it was easy to feel the stones on passing a finger through the internal meatus and so I extracted them through this route, thereby, I think, unduly stretching the bladder neck. Urinary leakage occurred on the fourth day and this soon became obviously infected. Twelve days after the operation, an abscess appeared over the gluteal region, which had to be evacuated.

These incidents do not detract from the merits of the operation, but rather serve to emphasize the necessity of adhering to the technique described by Mr. Millin. It is of importance to make certain that the catheter has been properly inserted into the bladder and that it does not become displaced whilst completing the operation.

The operation is perhaps technically more difficult than the suprapubic method, but can, nevertheless, be expeditiously accomplished. When the operation is completed, the after-treatment is simple and no specially trained team is required to carry it out.

Mr. Clifford Morson (in *absentia*, read by Mr. Ainsworth-Davis): There seem now to be almost as many techniques for prostatectomy as there are urologists in this country. The explanation is simple. Surgeons are dissatisfied with many of the end-results, and it is not to be wondered at when it is remembered how much damage is done to the urethra by the removal of the prostate. Surgery can never be the last word in the treatment of this disease. It is dangerous to dogmatize about the results of a new operation until it has had a fair trial, but I certainly like the simplicity and minimum of damage to surrounding tissues of Mr. Millin's technique. However, I cannot give whole-hearted support to it until I know what are going to be its remote results, and for this we must wait two years. In a ward of one of my hospitals there lie side by side suprapubic and retropubic cases. The only difference in the post-operative convalescence is the anxiety about the tied-in catheter blocking with a closed bladder. As for length of stay in hospital both are healed in about a fortnight, but he is a foolish surgeon who hurries his prostate cases out of hospital. I would remind you of the investigations of Semple and myself some years ago which showed that the rate of healing in the prostatic cavity was extremely slow, and many weeks after the abdominal wound had healed there was a raw surface. The extent of that raw area is reduced by a plastic operation such as Wildbolz's or Harris'. Now that is what affects the remote results. The more scar tissue there is uniting bladder mucous membrane to urethral mucous membrane the more urinary dysfunction there will be. Scar tissue contracts slowly so that the dysfunction may not manifest itself for a long time. I think that like the suprapubic operation, the retropubic will give good immediate results. An amazing change has come over the results of suprapubic prostatectomy in the last five years thanks to the complete control of bladder sepsis. Secondary hæmorrhage now is very rare.

Electrolytic sodium hypochlorite, the sulpha drugs, urea formic iodide, and now penicillin are all playing their part in reducing complications and the mortality rate. Professor Noordenbos of Amsterdam in a recent speech at the College of Surgeons stated that the introduction of penicillin had caused the greatest revolution in surgery since Lister. There is no reason to-day why any prostatectomy case in private practice should die of a urinary complication. In my last 40 cases in private practice I have not had a death. For the past 2 years I have had 60 cases at a municipal hospital with 2 deaths. It is notorious that many of these patients are poor surgical risks and yet they survive the operation. Mr. Irwin at St. Paul's is getting similar results.

Mr. Alex. E. Roche: The main advantages of Mr. Millin's operation are not its low mortality or the short period in bed—about two weeks. Similar advantages are claimed for perurethral resection and for Steinach II, which both have this advantage over Millin's operation, of avoiding a suprapubic incision.

Nor is the absence of suprapubic leakage of urine the main advantage of this operation. That, again, is shared by the perurethral resection and Steinach II, not to mention Harris's prostatectomy with closure.

No, the main advantage, it seems to me, is that, unlike perurethral resection and Steinach II, Millin's operation is radical.

The absence of mortality in 20 cases is good, but, of course, we all have runs of 20 or more prostatectomies without mortality. Personally I like to have, and I think I can achieve, a low mortality in my prostate operations—perhaps 5 to 7%. I do a two-stage Freyer-like prostatectomy—an operation which will, I think, last as long as prostatectomies are being performed.

With regard to nomenclature all suprapubic operations are retropubic when the patient is supine, but, whereas ordinary suprapubic prostatectomy is transvesical, Millin's is prevesical, so I prefer the term prevesical prostatectomy to retropubic prostatectomy.

Mr. John Everidge: I think too much has been said about spasms arising as the direct result of incision through the bladder wall. After all we do not see spasms after simple suprapubic drainage nor after partial cystectomy, &c., in either sex. A further factor must be necessary.

Mr. F. E. Feilden: In my view there is no one approach to the pathological prostate; each case must be considered on its own merits, and the appropriate route selected after careful pre-operative investigation. I do not think the post-operative pain referred

to by Mr. Millin is associated with either the indwelling catheter or the line of suture, but is due to incomplete hæmostasis.

The operation of retropubic prostatectomy is not one which should be done by the occasional prostatectomist. We all know of the appalling results associated with trans-urethral resection when performed by those not competent to do the operation. The same would occur in the operation of retropubic prostatectomy under similar conditions, and much unjustifiable discredit will be brought upon the operation.

Mr. H. P. Winsbury-White: I congratulate Mr. Millin upon his success with a new operation, especially in relation to hæmostasis, which is always a chief concern of every prostatectomist.

I was glad Mr. Millin had mentioned that, following the cystoscopic examination, he was prepared to proceed at once to either transurethral resection or prostatectomy, according to what he found. I, too, feel that this is a wise way to proceed, because there are certain cases in which the decision can only be arrived at by cystoscopy.

I cannot agree that it is not necessary to remove vesical diverticula. If these are left behind then infection of the bladder will remain, whereas one can look forward to a crystal-clear urine in due course for the majority of cases.

The question of post-operative obstruction is a real one with all types of prostatectomy, and I would like to know from Mr. Millin whether it is possible to remove the posterior margin of the prostatic bed by the retropubic route. I, personally, remove this shelf with the diathermy knife and feel that this procedure is an important safeguard.

Mr. Edgar Freshman asked whether Mr. Millin had found it helpful to use a special posterior blade with one of the standard automatic bladder retractors.

Mr. Millin (in reply): I take this opportunity of expressing my gratification at the reception accorded by so many urologists, not only here to-night but in correspondence from many parts of the world, to my retropubic operation. I had been prepared for more opposition. To the President I would say that the "subtle" form of post-operative obstruction he has met with so disastrously indicates no inherent fault of the operation but rather faulty technique—obviously careful inspection and palpation of the prostatic bed had not been carried out.

I do not agree with Mr. Riches that the vertical incision through the capsules is preferable in the case of the grosser enlargements; it may lead to an upward or downward splitting, so jeopardizing either internal or external sphincter. I still prefer the simple preputial suture for catheter fixation to one traversing the bladder. Unless extensive diathermic coagulation has been employed, cysto-urethroscopy on the eleventh post-operative day shows few if any sloughs, and discharge from hospital on the fourteenth day is safe. I agree with him on the desirability of minimizing the period of indwelling catheter and now aim to remove the tube on the third or fourth post-operative day.

On the question of post-operative spasms, I agree with those who believe that these are primarily due to clots in the bladder and I attribute the freedom from this complication in the operation to the absence of this factor.

To Mr. Winsbury-White I would say that it is simple and frequently desirable to resect a wedge from the posterior lip of the bladder neck in the retropubic approach.

Special instruments are not an essential, but a movable upper blade to the self-retaining retractor is a help.

Section of Physical Medicine

President—J. W. T. PATTERSON, M.D., F.R.C.P.Ed.

[December 12, 1945]

Observations on the Value of Electromyography in Lesions Involving the Lower Motor Neurone in Man

By GRAHAM WEDDELL, M.D.

In a previous communication to the Neurological Section of the Royal Society of Medicine (Weddell, 1943), a brief account was given of the technique and application of electromyography in clinical medicine. Since then, many more neurological affections have been investigated, as a result of which it has become possible to indicate more precisely the value of electromyography in the diagnosis and prognosis of lower motor neurone lesions.

In lesions where there is either destruction of the whole lower motor neurone, or degeneration of its axon, fibrillation action potentials can be recorded from the denervated muscle fibres. It is this characteristic change in the electrical activity of the muscle that can be used to distinguish between degenerative lesions of the lower motor neurone and affections in which the integrity of the neurone is preserved although the axon is temporarily incapable of conducting nervous impulses. For instance, in cases of facial paralysis, it has been possible to differentiate, by observing the presence or absence of fibrillation action potentials, between cases of Bell's palsy and those involving more severe damage to the facial nerve. Similarly, in certain cases of sciatica with muscle weakness and wasting, evidence has been obtained that the nerve has been partially destroyed. In such cases, the prognosis is not so favourable as in those in which no fibrillation action potentials can be recorded.

In peripheral nerve lesions, it is not claimed that electromyography should replace tests based on the electrically induced activity of muscles but that electromyography affords a more delicate means of assessing the condition of the motor nerve. It can detect minimal degrees of lower motor neurone denervation and the earliest stages of muscle reinnervation.

In two cases of aphonia, which were diagnosed as being due to idiopathic recurrent laryngeal nerve palsy, the vocal muscles contracted normally, and no fibrillation action potentials were recorded from them. In each of these cases, the affection was found to be due to arthritis of the arytenoid joint.

These investigations have been reported *in extenso* in *Brain* (1944).

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The Value of Electromyography in Lesions Involving the Lower Motor Neurone

By RUTH E. M. BOWDEN, M.B., B.S.

DR. WEDDELL and his colleagues, Drs. Feinstein and Pattle, have made clinical electromyography possible and have done much to evaluate the findings in different disorders of the lower motor neurone. Electromyography marks a notable advance in diagnostic methods, and it can now be considered an essential aid to research in these diseases, but it is not equally certain that it is suitable for routine clinical examinations.

to by Mr. Millin is associated with either the indwelling catheter or the line of suture, but is due to incomplete hæmostasis.

The operation of retropubic prostatectomy is not one which should be done by the occasional prostatectomist. We all know of the appalling results associated with transurethral resection when performed by those not competent to do the operation. The same would occur in the operation of retropubic prostatectomy under similar conditions, and much unjustifiable discredit will be brought upon the operation.

Mr. H. P. Winsbury-White: I congratulate Mr. Millin upon his success with a new operation, especially in relation to hæmostasis, which is always a chief concern of every prostatectomist.

I was glad Mr. Millin had mentioned that, following the cystoscopic examination, he was prepared to proceed at once to either transurethral resection or prostatectomy, according to what he found. I, too, feel that this is a wise way to proceed, because there are certain cases in which the decision can only be arrived at by cystoscopy.

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On the question of post-operative spasms, I agree with those who believe that these are primarily due to clots in the bladder and I attribute the freedom from this complication in the operation to the absence of this factor.

To Mr. Winsbury-White I would say that it is simple and frequently desirable to resect a wedge from the posterior lip of the bladder neck in the retropubic approach.

Special instruments are not an essential, but a movable upper blade to the self-retaining retractor is a help.

Using the standardized technique it was the exception to find the return of voluntary contraction before return of excitability to the stimuli of 1/1000 second duration. In the majority of these (all of whom were recovering from complete degenerative nerve lesions) it was possible to make a comparison of the merits of the electrical reactions and the electromyogram (unpublished work). There is conclusive evidence that the electromyogram is superior to the electrical tests in the detection of early reinnervation, and it has the added advantage of being performed more rapidly. Isolated observations by either method are, however, of limited value; the findings on one occasion of a response to a short duration percutaneous stimulus is no proof of innervation, and it is possible to find a feeble and localized contraction with an unusually high threshold to faradism in totally denervated muscle. Where recovery is taking place satisfactorily there is a progressive improvement in excitability. Similarly, the finding of a few motor unit action potentials is no guarantee of functional recovery, it only signifies that some axons have reached the muscle and established functional connexion with muscle fibres. If reinnervation is progressing satisfactorily, there is a corresponding improvement in the number of motor unit action potentials in any particular muscle and, furthermore, the more distal muscles show evidence of reinnervation in anatomical order. The time-lag between the return of motor unit action potentials and voluntary contraction is dependent upon the type of lesion in the nerve (unpublished work).

TREATMENT

Treatment is dependent upon the type of lesion. Degenerative lesions require physiotherapy even if operative intervention is not necessary. In the palsies involving the intrinsic muscles of the hand, it is imperative to prevent atrophy as far as possible. E. C. S. Jackson (1945*a, b*), has shown that the rate of atrophy is rapid in the early days after injury, the volume of the muscles is not restored in the absence of reinnervation. Galvanic stimulation, given in regular and adequate doses, was effective in retarding the early rapid wasting but could not wholly prevent it and, in the later stages, treatment maintained the volume of the hands. In suitable cases (regrettably few) it may be possible to suture the nerve within three weeks of injury, and, therefore, from the point of view of physiotherapy and operative repair, early diagnosis of a degenerative lesion is essential.

At the moment there is no method of determining the state of the nerve at the site of the lesion; it is only possible to diagnose the presence of a complete or partial degenerative or non-degenerative lesion of a nerve. It is always possible to watch the progress of a case, the earliest sign of motor recovery being the appearance of the motor units but this may be undesirable since, if the lesion is a high one, such delay may prejudice recovery should repair be necessary. If a nerve lesion is associated with an open wound on the course of the nerve, or there is a fracture in which there is likelihood of compression or serious damage to the nerve trunk, the findings of a few motor unit action potentials should not be taken as a guarantee of useful function. It may be justifiable to wait for a few weeks, particularly if the lesion is a low one, or associated with injuries where experience shows the prospects are good. However, unless there is reasonably rapid improvement in the number of motor units and evidence of orderly reinnervation of the muscles, exploration should not be delayed. In several instances motor units have been found where only a shred of the nerve trunk remained intact in such cases.

In the light of present knowledge of peripheral nerve injuries, it does not seem possible to abandon any of the available diagnostic methods. The electromyogram is a useful aid to diagnosis, prognosis and treatment. If used in conjunction with information given by the history and full clinical examination, it is possible to make a fairly accurate and comprehensive diagnosis in the majority of cases; but there is still a small group in which the surgeon is faced with the problem, "Is it best to wait and see, or should one look and see without further delay?" Early exploration is indicated if there is any doubt about the ultimate progress of the patient.

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In a study of peripheral nerve injuries admitted to the centre under the care of Professor H. J. Seddon, some points have emerged that merit discussion. The problems can be considered under the headings of diagnosis, prognosis and treatment.

DIAGNOSIS

It has been suggested that electromyography has outmoded investigation of electrical reactions of the affected muscles. The results of electrical reactions have been described as unreliable, but the methods used have often lacked uniformity and it is not, therefore, possible to evaluate them adequately. Recently stimulators have been designed by Bauwens (1941), Ritchie (1944), Grey Walter and Ritchie (1945), which enable the clinician to make comparable observations.

In this investigation the stimulator designed by Bauwens has been used. Three durations of stimulus are available, 1/1000, 1/50 and 1 second; the impulses are of square wave form and are delivered at a known constant current which may be selected by the observer. The intensity of the stimulus may be varied independently of duration. A series of patients has been studied using both electromyography and the electrical reactions which were obtained by a standardized technique.

(a) *Degenerative lesions*.—Only 14 cases were seen within thirty-five days of injury, 7 within fourteen days. Using the electrical reactions, conclusive evidence of a degenerative lesion of the nerve was obtained within four to ten days. Nerve conduction distal to the lesion had failed by the third or fourth day, and the reaction of denervation was fully established by the fifteenth day. The earliest fibrillation irritability was seen on the sixth day, and the earliest fibrillation seen was observed on the thirteenth day, more commonly it was not established until after twenty days, in 1 case only after forty-four days. In none was it vigorous before the twentieth day. Motor unit irritability may be found up to about twenty-eight days after injury in the presence of a complete degenerative nerve lesion.

(b) *Non-degenerative lesions*.—*Neurapraxia* (Seddon, 1942): Nerve conduction remains below the lesion, which is in the nature of a block to conduction of impulses. In a man with a lesion that was mainly one of neurapraxia, seen two months after injury, the electrical reactions were comparable with normal, and nerve conduction was present, but there was gross weakness. Electromyography showed a partial lesion, a few motor units and one or two spikes of fibrillation were present. The information given by this alone could not allow of a confident prognosis being given. With the data from both investigations it was possible to give a fairly exact prognosis. In another case of partial axonotmesis and neurapraxia which was seen early after injury, nerve conduction was present eight days after injury, the electrical reactions varied (it is possible that this is not without significance). It was, however, permissible to diagnose the nature of the lesion from these findings, and electromyography provided confirmation. The subsequent progress of the case showed the accuracy of the diagnosis.

(c) *Anomalous innervation*.—This is not uncommon in the hand, it is one of the pitfalls in diagnosis and may lead to serious delay in repair of severed nerves. Electromyography will demonstrate the presence of the innervated and denervated muscle fibres, but cannot give any indication of the origin of the intact nerve fibres. Electrical stimulation of the appropriate nerve trunks can give the necessary information rapidly. An illustrative case may be quoted. An officer had a gunshot wound of the elbow with complete loss of sensibility of ulnar distribution. All the ulnar intrinsic muscles were acting but very weak. Electrical reactions and electromyography indicated a partial degenerative lesion. Ulnar nerve stimulation at the wrist was positive, median nerve stimulation at the wrist was negative for the hypothenar and interosseous muscles. Ulnar nerve stimulation at the elbow above the lesion was negative. At operation a completely severed ulnar nerve was found and sutured, anomalous fibres from the median nerve having entered the ulnar nerve trunk in the forearm. Electrical reactions (which should always include stimulation of the nerve trunks) give evidence of degenerative lesions earlier than electromyography, and they can solve the difficulties of anomalous innervation in a way that cannot be expected of electromyography.

PROGNOSIS

It is generally agreed that electrical reactions are wholly unreliable in prognosis but it is noteworthy that, amongst others, Head and Sherran (1905) and Benisty (1918) reported that in some cases faradic excitability returned before voluntary contractions.

Using the standardized technique it was the exception to find the return of voluntary contraction before return of excitability to the stimuli of 1/1000 second duration. In the majority of these (all of whom were recovering from complete degenerative nerve lesions) it was possible to make a comparison of the merits of the electrical reactions and the electromyogram (unpublished work). There is conclusive evidence that the electromyogram is superior to the electrical tests in the detection of early reinnervation, and it has the added advantage of being performed more rapidly. Isolated observations by either method are, however, of limited value; the findings on one occasion of a response to a short duration percutaneous stimulus is no proof of innervation, and it is possible to find a feeble and localized contraction with an unusually high threshold to faradism in totally denervated muscle. Where recovery is taking place satisfactorily there is a progressive improvement in excitability. Similarly, the finding of a few motor unit action potentials is no guarantee of functional recovery, it only signifies that some axons have reached the muscle and established functional connexion with muscle fibres. If reinnervation is progressing satisfactorily, there is a corresponding improvement in the number of motor unit action potentials in any particular muscle and, furthermore, the more distal muscles show evidence of reinnervation in anatomical order. The time-lag between the return of motor unit action potentials and voluntary contraction is dependent upon the type of lesion in the nerve (unpublished work).

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[January 9, 1946]

The Detection and Evolution of Adolescent Deformities of the Spine

By F. H. KEMP, M.R.C.P.

IN 1941 Dr. D. Wilson drew my attention to a paper by Shortt and his colleagues (1937) describing dental fluorosis associated with skeletal changes in the inhabitants of certain villages in the Madras Presidency. This aroused my interest in common disorders of the spine as the clinical picture is in many way similar to the type of ankylosing spondylitis (Marie Strümpell) which we see in this country but the radiographic changes are totally unlike. Thus, the first signs of general intoxication begin when the individual is about 30 years old, evidenced by a tingling in the limbs and in the body generally. Pain and stiffness increase until the entire spine, including the cervical region, behaves like a continuous column of bone. There is stiffness of other joints and ossification of the periarticular tissues, tendinous insertions and the interosseous fascia. By the time the condition is fully developed the patient is about 40 years old; there is much cachexia and death ensues from intercurrent disease. There are many minor variations and all cases in a village do not exhibit the same degree of intoxication. The amount of fluorine in the drinking water responsible for these changes was between 3 and 4 parts per million. Similar changes due to fluorine in the drinking water have been reported by Ockersse (1941) in African natives, and by Lyle in China (1946).

The evidence that these changes are really due to fluorine is conclusive. The radiographs show changes exactly similar to those described by Flemming Møller and Gudjonsson (1932) in cryolite workers and by Wilkie (1940) in workers in a Sheffield factory producing aluminium fluoride and hydrofluoric acid. Experimentally, similar changes have been produced by feeding fluorine to animals (Roholm, 1937).

These studies are specially important since they prove that in certain circumstances very profound effects on the skeleton may be excited by substances normally present in food and drink. The quantity of fluorine present in the drinking water necessary to cause these changes is no greater than is found in some waters in some parts of England. Why do we not see these changes in this country?

It seems that the development of the disease is influenced by several factors. Pundit and his colleagues (1940) found that bone changes in fluorosis bore a definite relationship to the economic and nutritional states of the communities. Nowhere in England are the social conditions so unsatisfactory as are those of the native population in the parts of the world where endemic skeletal fluorosis has been described.

In 1942, Dr. Wilson and I published the findings of a similar investigation amongst the inhabitants of Oxfordshire villages. Dental fluorosis, revealed by mottling of the enamel, is very common; there were some very severe cases. We found no evidence of skeletal fluorosis, but there was a remarkable incidence of changes in the spines of the children—of the type described by Scheurmann (1921 and 1936) as "kyphosis dorsalis juvenilis". We continued our investigations (*Lancet*, 1942) and found that these changes were very common. In one school at least a third of the children were affected. We tried to correlate the changes with incidence and severity of the dental fluorosis, but we were unable to prove conclusively that they were related. The worst cases were seen in the lower social classes or in children where there was a history of defective nutrition in the early years. A group of poor Oxford city children (the incidence of dental fluorosis in Oxford city is very low) showed no changes.

The fact which was most surprising was that most of these children had no complaints, yet many were very deformed. As a rule, the changes were confined to the lower six dorsal vertebrae, but in some cases the mid-dorsal region was involved and one or two showed changes in the upper dorsal. There was a variable degree of deformity. Some cases with extremely severe changes had a perfectly normal appearance of the spine clinically, others had a well-marked rounded kyphosis in the affected area. In some cases, only a single vertebra was wedged. It is our view that the presence or absence of deformity is conditioned partly by the natural postural habits of the individual, partly by gravitational influence and partly by the severity of the changes and the degree of softening of the vertebrae.

When we were doing this work, it occurred to me to inquire whether such changes persisted in later life. I had lateral radiographs taken of the chest of a number of medical students and student nurses at the time when they came forward for



(a) Radiograph showing marked irregularities of some of the end-plates and a spur of bone projecting from the anterior surface of the body of D.12.



(b) Second radiograph of the same area taken twelve months later, showing that the progression of the change has reached forward and included the spur of bone shown in the first radiograph.



(c)



(d)

(c) and (d) Other portions of this boy's spine showing an astonishingly irregular distribution of the changes.

FIG. 1.—Four radiographs of the same boy (G. L.) showing severe osteochondrosis of the end-plates. This boy has been watched for four years, during which time he has had no symptoms.

[January 9, 1946]

The Detection and Evolution of Adolescent Deformities of the Spine

By F. H. KEMP, M.R.C.P.

IN 1941 Dr. D. Wilson drew my attention to a paper by Shortt and his colleagues (1937) describing dental fluorosis associated with skeletal changes in the inhabitants of certain villages in the Madras Presidency. This aroused my interest in common disorders of the spine as the clinical picture is in many ways similar to the type of ankylosing spondylitis (Marie Strümpell) which we see in this country but the radiographic changes are totally unlike. Thus, the first signs of general intoxication begin when the individual is about 30 years old, evidenced by a tingling in the limbs and in the body generally. Pain and stiffness increase until the entire spine, including the cervical region, behaves like a continuous column of bone. There is stiffness of other joints and ossification of the periarticular tissues, tendinous insertions and the interosseous fascia. By the time the condition is fully developed the patient is about 40 years old; there is much cachexia and death ensues from intercurrent disease. There are many minor variations and all cases in a village do not exhibit the same degree of intoxication. The amount of fluorine in the drinking water responsible for these changes was between 3 and 4 parts per million. Similar changes due to fluorine in the drinking water have been reported by Ockerse (1941) in African natives, and by Lyle in China (1946).

The evidence that these changes are really due to fluorine is conclusive. The radiographs show changes exactly similar to those described by Flemming Møller and Gudjonsson (1932) in cryolite workers and by Wilkie (1940) in workers in a Sheffield factory producing aluminium fluoride and hydrofluoric acid. Experimentally, similar changes have been produced by feeding fluorine to animals (Roholm, 1937).

These studies are specially important since they prove that in certain circumstances very profound effects on the skeleton may be excited by substances normally present in food and drink. The quantity of fluorine present in the drinking water necessary to cause these changes is no greater than is found in some waters in some parts of England. Why do we not see these changes in this country?

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FIG. 4.

FIG. 4.—Radiograph of the lower dorsal spine of a young woman, aged 38 years, showing wavy outlines of the anterior edges of the vertebral bodies. This is one of the early features of a not uncommon type of osteomalacia.



FIG. 5.

FIG. 5.—Radiograph of a woman aged 67 years, showing only slight deformity and practically normal radiographic appearances; thus proving that structural abnormalities are not the inevitable accompaniment of old age.

The 75 cases of dorsal kyphosis show a variety of radiographic appearances; the kyphosis in some cases was due to wedging of the vertebral bodies, in others to diminution in the disc space, while in some it was due to both. There were other changes which indicated that the group was comprised of cases of mixed aetiology, but the range of appearances at the different age levels was such that one could draw no clear distinction between adolescent and senile cases. Thus, many cases conforming to the description given by Beadle (1931) of senile kyphosis were seen in young adults of both sexes.

The experience I gained from this work forced me to the view that many conditions of the spine which we are accustomed to attribute to old age are really the results of progressive degeneration throughout the years, of malformations acquired in youth. Furthermore, as these changes are so common, they should not be accepted as the cause of a patient's symptoms without a critical examination of all the features of the case. Thus, it is common practice to see patients who have been previously diagnosed as arthritis of the spine on the basis of an X-ray examination, whose subsequent history reveals that they were really suffering from some other complaint.

How are we to classify these patients? I am satisfied with the broad division into those which have functional and those which have structural defects. As a radiologist, I am primarily concerned with the latter group, but I cannot ignore the former since we know that the internal configuration and external shape of a bone change with any constant change in the stress applied; so that it will be best adapted mechanically to resist the stresses placed upon it (Wolff's Law). In the structural group, I feel that we should describe the changes as we see them, in words that do not imply their aetiology. I am opposed to grouping all kinds of different structural conditions under the heading "arthritis deformans", as, for instance, in a recent textbook on orthopaedics, where the title "arthritis deformans" covers a composite picture of a variety of conditions including ankylosing spondylitis. This only leads to confusion.



FIG. 2.—Severe deformity in a young medical student of 19 years, who had no knowledge of his deformity.



FIG. 3.—Medical student aged 19 years. A very unusual compensatory lordosis associated with a simple wedging of the upper dorsal bodies.

their routine chest examinations. These showed a surprising number of changes. Many had irregularities of the end-plates, wedging of the vertebral bodies and quite pronounced deformities. Several young men and women had very marked lipping of the vertebrae, such as one had hitherto associated with advanced old age. I had to question these people very carefully (in order not to raise alarm), but I was able to ascertain that only one of them had any symptoms and this was a young nurse who had, in addition, some scoliosis. Another surprising fact was that they were unaware of the deformities. One young man, aged 19, had a very severe dorsal kyphosis of which he knew nothing. In many cases, the radiographic features of these lesions suggested that they were the healed effects of osteochondrosis of the end-plates (Scheurmann's disease), but others might have been due to long-standing postural errors. These views were confirmed when I was able to do a second examination of some of the children. In some, who had little deformity, the changes had practically disappeared, but others showed changes like the students. (See figs.)

I was also interested to find out how many cases at different age-groups I saw in hospital practice. To answer this question, I reviewed all the radiographs of the dorsal spine which were taken for orthopaedic out-patients for the years 1938/1942 inclusive (Table I, p. 346). I excluded all cases of manifest organic disease such as tuberculosis, secondary neoplastic deposits and ankylosing spondylitis, also cases of gross scoliosis. I tabulated the others according to whether there was a manifest clinical dorsal kyphosis or not. "Normal" was used very liberally to include any case where there was doubt as to the deformity, as well as cases showing irregularities of the end-plates, and marginal lipping which did not have a dorsal kyphosis. From the table it will be seen that our experience is not only limited but selective. It seems very unlikely that the numbers we see are representative of the true incidence of dorsal kyphosis at the different age levels. It will be noticed that the greatest number of patients were seen between the ages of 10 and 40 years, which can only mean that it is customary for the practitioners to pay more attention to complaints of the young people. Notice our very limited experience of the normal.

Section of Odontology

President—LILIAN LINDSAY, L.D.S. Durham, L.D.S. Ed.

[January 28, 1946]

Arterial Supply of the Mandible

By ALEXANDER MACGREGOR, M.A., M.D., M. and L.D.S. R.C.S.

It is, of course, a common observation that necrosis of large fragments of bone following fracture of the mandible is an uncommon sequela save in the presence of gross comminution and sepsis.

The main arterial supply of the mandible is derived from the inferior dental artery on each side and, according to the older writers, there was little anastomosis across the mid-line of the mandible. The survival of fragments of bone following fracture was in consequence assumed to be entirely due to the arterial supply derived from the numerous muscular attachments to the bone.

Little work has been done to verify the assumption that there was no anastomosis of the two inferior dental arteries across the mid-line: but in 1935 Howkins published the result of his studies in the *Proceedings of the Royal Society of Medicine*. As a result of this work he formed the conclusion that in pigs, monkeys and humans there was little if any anastomosis past the mid-line of the mandible, though it was present in the lips and neighbouring area, probably from anastomosis of the mental and facial arteries.

An opportunity to test this view that no anastomosis of the two inferior dental arteries across the symphysis of the mandible existed, occurred when a patient who had had a fracture in the $\overline{6}$ region died eight days after the injury. The mandible was removed post mortem, stripped of its muscular attachments and, with the aid of a cannula in each of the two inferior dental arteries, a differential arterial injection was performed on each side. Using the ordinary technique, after tying in the cannulae the blood-vessels were well washed out with normal saline. The mandible being held under warm water carmine gelatin in a warm and liquid state was then injected through the cannula into the inferior dental artery of the intact side of the mandible, and trypan blue gelatin was injected into the fractured side. The gelatin was allowed to set, and the mandible split and cut in sagittal section.

It was at once apparent that the trypan blue gelatin extended to the site of fracture in the blood-vessels of the posterior fragment of the left side, and carmine gelatin was present in those of the right side and left side as far back as the site of fracture. It was, therefore, clear that an anastomosis across the mid-line must have been present to allow the carmine gelatin to travel backwards to the fracture area. (A colour photograph of the mandible was taken and this was shown at the Meeting.)

It is not suggested that the muscular attachments of the mandible do not play a most important part in the survival of mandibular fragments following fracture. It is clear that following a bilateral fracture of the mandible with displacement such that both inferior dental arteries must have been severed, the survival of the anterior fragment could not depend upon the inferior dental arteries. It is, however, suggested that this anastomosis of the inferior dental arteries across the mid-line which is present—at any rate eight days after injury—may assist in the survival of parts of the bone, and that the older view that anastomosis across the symphysis does not occur appears, therefore, to be incorrect.

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APRIL—ODONT. 1

I now hope to collaborate in an investigation designed to observe the growth and development of 1,000 children. This will take a lifetime to complete but it should afford an answer to many problems, including some of those relating to the spine.

TABLE I.

Year	Dorsal kyphosis							Normal						
	0-9	10-19	20-29	30-39	40-49	50-59	60-69	0-9	10-19	20-29	30-39	40-49	50-59	60-69
1938	1	11111	11	111		1	11	1	1111	1				
1939	11	1111	11	1111	1	11	1		1111		1111	11	1	1
1940	1	11	1111	11111	1	11		11	11	111	1		1	1
1941		11	1111	1111	1	1111	11111	111	1111	1	111	1	1	
1942		11	111	11	1		1							
Total	4	15	16	18	4	9	9	6	14	5	8	3	3	2
Grand total = 75.							Grand total = 41.							

CLASSIFICATION OF DORSAL KYPHOSIS

- (1) Kyphosis without structural changes, i.e. functional.
 - (2) Kyphosis (a) with wedging of the vertebral bodies.
(b) with regular ossification of the end-plates.
(c) with natural disc spaces.
 - (3) Kyphosis (a) with or without wedging of the vertebral bodies.
(b) with general narrowing of the disc spaces.
(c) with regular ossification of the end-plates.
- This may progress so that ultimately there are no disc spaces, resulting in pressure contact between the vertebrae and sclerosis of the architecture of the bodies.
- (4) Kyphosis (a) with or without wedging of the vertebral bodies.
(b) with narrowing of the anterior third of the disc spaces.
(c) with sclerosis of the anterior third of the margins of the end-plates.

This condition may progress until there is calcification in the interior third of the disc and finally bony fusion. (Schmorl's anterior necrosis of the discs.)

- (5) Kyphosis with softening of the vertebral bodies, i.e. osteomalacia.
Type A is characterized by a gradual but progressive wedging of the vertebral bodies and results in a smooth rounded kyphosis.
Type B is seen in older subjects. Characterized by collapse of one or a number of vertebral bodies and decalcification of all the bones.
- (6) Kyphosis associated with osteochondrosis of the end-plates (Scheurmann's disease). This condition is not invariably associated with kyphosis.

Other common associated conditions are:

- (1) *Schmorl's nodes*.—Herniation of the nucleus pulposus into the vertebral body may complicate or aggravate any of the above-mentioned conditions but it is doubtful whether it is a primary causal factor in any of them.
- (2) *Marginal lippling*.—This may be regarded as a reaction to strain.

As a sequel to any of these changes there may be other changes in the spine:

- (1) Changes in the lateral articulations—osteoarthritis.
- (2) Changes in the sacro-iliac joints—osteoarthritis.
- (3) Contact between the spinous processes (usually in the lumbar region on account of the associated lordosis).
- (4) Moulding and elongation of the spinous processes, sometimes, but rarely, associated with local symptoms—a clinical state resembling clay-shoveller's syndrome.
- (5) Changes in the costo-vertebral articulations—osteoarthritis. Often present, rarely severe.

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tissue, but under the microscope there cannot be the slightest doubt that the plexus is located within the epithelium.

The rodents in this communication are represented by the rabbit, rat, and mouse. In each of these animals Types I, II, and III were found, and in the rat and rabbit Type IV fibres were also seen. Type II B fibres were particularly conspicuous in the animals of this order. They have a relatively short intra-epithelial course and appear to end in the deeper part of that tissue. They do not have specialized end-organs (Plate I, figs. 8, 9, 10).

In the rabbit Type IV fibres pass out into the superficial part of the epithelium but they do not reach the stratum corneum. These fibres terminate in knob-like swellings (Plate I, fig. 4). It will be observed that the fibres illustrated in this photomicrograph have a wavy intracellular course; in one case this is so marked that the fibre has a distinct loop as the fibre passes towards the periphery.

In the rat the sub-epithelial connective tissue of the gum is particularly well supplied with nerve fibres, which form large nerve plexuses, that cannot be easily divided into deep and superficial plexuses. It is from these that the Type III fibres arise (Plate II, fig. 11).

In the mouse intra-epithelial fibres were found with a peculiar distribution that we have been unable to find in any other animal. On entering the epithelium they bend sharply and run for some distance, parallel to the epithelial-connective tissue boundary, but lie wholly within the former tissue (Plate II, fig. 12).

In this animal (Plate II, fig. 14), we found a definite intra-epithelial anastomosis. A fibre of moderate thickness enters the epithelium and divides into several finer fibres; a second fibre, not shown in this photomicrograph, enters the epithelium a little distance away from the other one and joins with it to form a distinct network. This structure differs from the one described in the mole, earlier in this paper, because in this specimen a definite anastomosis of the fibres occurs. As far as we know, such an intra-epithelial plexus has not been previously described.

In the ferret all five types of intra-epithelial fibres were found, except that II A took the place of II B. Types I to IV resemble those described earlier, and therefore require no further description. The coils were of the V B variety and are shown in Plate II, figs. 15 and 16. From the coils single intra-epithelial fibres arise, which sometimes could be traced to the stratum corneum. In one example the nerve ends with a knob-like swelling, in the other this is absent. We were unable to satisfy ourselves that the bulbous ending was not located within a cell.

In the next portion of this paper, which deals with the innervation of the human gum the description will be extended to include certain intra-papillary endings that have not previously been described. The first of these can be seen in Plate II, figs. 19 and 20. It is situated in the tip of the papilla, and forms an elongated club-like swelling. It occurs at the termination of a thick fibre, which, after a meandering course through the papilla, terminates in this end-organ. The nerve ending is made up of a very distinct neuro-fibrillar network, and gives origin to no intra-epithelial fibres. In its shape it resembles the club-like ending described by Botezat, and photographed by us in the mole (1939a, fig. 3). There is this difference, however; in the mole the end-organ lay within the epithelium. In the camera lucida reconstruction (Plate II, fig. 20) the end-organ is more extensive than in the photomicrograph (Plate II, fig. 19). The reason for this discrepancy is that the end-organ extended to the sections on either side of the one shown in fig. 19, and therefore the complete end-organ can only be seen in the reconstruction which was made from these three sections.

The second of the new intra-papillary structures is illustrated in Plate III, fig. 23. It consists of a single fibre which arises from the nerves of the sub-papillary region. From this region it runs through the papilla and near its apex forms a loop. As it ascends in the papilla it lies close to the epithelium, but at the apex it lies a short distance away from the border of this tissue. In this example, the fibre, as it descends towards the base of the papilla after forming the loop, divides into two fibres, but after a short course these reunite. This division and reunion have not been seen in other loops of a similar nature.

A single example of another type of intra-papillary loops has been seen (Plate III, fig. 24). A number of thick and thin fibres from the sub-papillary space ascend into the papilla; form loops in the tip of this structure, below the epithelium, and then pass backwards on the opposite side of the papilla to run towards the sub-papillary region.

From neither type of loop did intra-epithelial fibres arise. The sections on either side of those containing these structures were carefully examined, and no sign of any such fibres could be found.

To return to the innervation of the epithelium: Kadanoff in 1928 mentions that some human intra-epithelial nerve fibres pass through the tips of the papillæ and arise princi-

A Comparative Study of the Innervation of the Epithelium of the Gum

By W. LEWINSKY, M.D., and D. STEWART, D.Sc., L.R.C.P., M.R.C.S.

From the Department of Anatomy, Victoria University, Manchester

In previous papers we have discussed the innervation of the sub-epithelial tissue of the gum in some of the mammalian orders; and have also given a detailed account of the nerve supply of the epithelium of this tissue in man and the mole. In this paper we propose to describe comparatively the innervation of the epithelium of the gum in sheep, mole, rabbit, rat, mouse, ferret, and man.

The only previous paper on this subject is one by Jurjewa (1913). In it she discusses the innervation of the gum generally without special references to specific animals.

Our material was stained by the modification of Cajal's method devised by Gooding and Stewart (1937). After staining, the specimens were embedded in paraffin and cut into serial sections 12 μ thick.

Examination of the preparations showed that the intra-epithelial nerve fibres varied considerably in their origin from the sub-epithelial nerves, but it was possible for purposes of description to divide these origins into five distinct groups.

These are: Plate I, fig. 1:

Type I: Single fibres arising from bundles in the deeper layers of the connective tissue and running directly into the epithelium.

Type II α : Single fibres arising as in Type I but running for a distance along the epithelial connective tissue border, before they enter the epithelium.

Type II β : Several fibres having an origin and course similar to the single fibres in Type II α .

Type III: Fibres arising from superficial sub-epithelial plexuses.

Type IV: Fibres arising from intra-papillary plexuses.

Type V α : Several fibres arising from large intra-papillary coils situated at the apices of the papillae.

Type V β : Single fibres arising from small close coils also situated at the apices of the papillae.

The intra-epithelial nerves vary in thickness and can be classified as thick and thin fibres. The majority of the fibres fall into the thin group and have a wavy course as they run through the epithelium. The thicker fibres tend to have a much straighter course, frequently taper and sometimes divide as they run towards their termination.

On our examination of the preparations we found that there was a good deal of variation from animal to animal as to the presence or absence of the above-mentioned types of origin. Types I and II, however, were always present.

In the sheep only Types I and II were seen. In this animal the intra-epithelial fibres were all very thin and occasionally divided into two or three branches, but never into a greater number. These fibres end at different levels in the epithelium, which in the sheep is remarkably thick. Some of the fibres have a very long course and can be traced to the stratum corneum. They are usually wavy on account of winding through the intra-cellular spaces. They may either terminate with knob-like swellings, or many end freely without having any specific end-organs. Plate I, fig. 2, shows an example of these fibres.

In the mole Types I, II and III were present, and the greater number of the intra-epithelial fibres belonged to Type I. These varied in calibre from thin to thick. Type II were also frequently seen and they also varied in the thickness of their diameter (Plate I, fig. 3). As a variety of Type I, fibres arose from a leash-like structure in the sub-epithelial tissue, which is characteristic of the mole and has already been described by us and figured in an earlier paper (1939*a*, Plate I, fig. 2).

The intra-epithelial fibres as in other animals either end freely or terminate with knob-like swellings. There is, however, a third type of ending which is very characteristic of the mole, namely the Merkel-Ranvier touch meniscus (Plate I, fig. 6).

In the mole we have found nervous networks within the epithelium an example of which is shown in Plate I, fig. 7. This structure is formed by Type I fibres seen on the right of the photomicrograph, while on the left Type II fibres will be noticed entering one of the epithelial processes and forming a plexus therein. From these II β fibres branches arise, which break up and ramify within the apex of the process. Unfortunately the photomicrograph does not clearly differentiate off the epithelium from the connective

tissue, but under the microscope there cannot be the slightest doubt that the plexus is located within the epithelium.

The rodents in this communication are represented by the rabbit, rat, and mouse. In each of these animals Types I, II, and III were found, and in the rat and rabbit Type IV fibres were also seen. Type II b fibres were particularly conspicuous in the animals of this order. They have a relatively short intra-epithelial course and appear to end in the deeper part of that tissue. They do not have specialized end-organs (Plate I, figs. 8, 9, 10).

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A single example of another type of intra-papillary loops has been seen (Plate III, fig. 24). A number of thick and thin fibres from the sub-papillary space ascend into the papilla: form loops in the tip of this structure, below the epithelium, and then pass backwards on the opposite side of the papilla to run towards the sub-papillary region.

From neither type of loop did intra-epithelial fibres arise. The sections on either side of those containing these structures were carefully examined, and no sign of any such fibres could be found.

To return to the innervation of the epithelium: Kadanoff in 1928 mentions that some human intra-epithelial nerve fibres pass through the tips of the papillae and arise princi-

pally from coils situated in the tips of the papillae. Others take their origin from the loose papillary coils (intra-papillary plexuses), and a third group come from fine networks lying alongside the cells lining the papillae. The first two groups correspond to our Types IV and V, but the third has never been seen by us. In 1938 we described the intra-epithelial fibres belonging to Types II, IV, and V, which were also described by Bradlaw (1939). Since that date we have been able to find all five types of origin in the human gum.

In the photomicrographs accompanying this paper four of the five types are demonstrated. In Plate III, fig. 21, an example of Type I can be seen. Careful examination of the section in which this fibre occurred, and also of the adjoining sections, proved that no intra-papillary coils were present but only the missing intra-papillary part of the fibre; this fibre arose directly from a sub-epithelial nerve bundle, without the intervention of a sub-epithelial plexus. It will be noticed that the fibre terminates with a knob-like swelling in the stratum corneum. In this example the fibre is one of medium thickness, but thin fibres with a similar origin are frequently seen. These latter may enter the epithelium either at the tip or from the sides of the papillae.

Type II_A fibres have been frequently found in the human gum, and a specimen of this type can be seen in Plate II, fig. 17. These fibres arise either from the sub-epithelial nerve or sub-epithelial plexuses. They sometimes divide dichotomously inside the epithelium, and usually have knob-like swellings at their terminations (Plate III, fig. 25). In a former publication we figure an example of Type II_B fibres (1938, Plate II, drawing 2), but at that time its significance was not understood.

In an earlier paper (1939*b*) we noted the presence of superficial and deep sub-epithelial plexuses, but at that time we did not see any intra-epithelial fibres taking origin from these structures. Since then we have observed one example of these Type III fibres in man, and this is shown in Plate III, fig. 22. This photomicrograph demonstrates the presence of a sub-epithelial plexus from which arises one fibre that divides into three branches: The first branch is a long fibre, which runs along the borderline between epithelium and connective tissue, and at no point in its course does it enter the former tissue. The second branch is a Type III fibre, which enters the epithelium; although in this section its intra-epithelial course can only be followed for a short distance, in the adjoining sections its whole intra-epithelial distribution can be made out. Only a small portion of the course of the third branch can be seen; it runs along the border of the epithelium and the connective tissue, and its course resembles that of the first branch.

Type IV fibres have been described and figured in earlier communications (1938, Plate II, fig. 4 and 1939*b*, camera lucida drawing). In these papers, following the example of Kadanoff (1928), the structures we now call intra-papillary plexuses were then termed loose coils. We prefer the name plexus, because these structures form networks occupying the greater part of the papilla, and in no sense of the word can it be said that their fibres become coiled.

We have previously described two types of close coils, which were also seen by Bradlaw. The first was relatively large, and no intra-epithelial fibres arose from it; the second type was smaller, and gave origin to isolated nerve fibres of moderate thickness (Type V_B). We have since met with a third type of coil shown in Plate III, figs. 26 to 30 (Type V_A). This structure is a large loose coil and is not plexiform. It is further differentiated from the intra-papillary plexus by occupying only the upper third or quarter of the papilla. It differs from the coils previously described by being larger and looser, and by having neuro-fibrillar networks in its structure. These networks under lower magnification appear as swellings on the thicker nerve fibres; if, however, these swellings are examined under higher magnification, they are found to consist of fine networks, similar to those seen in Merkel's discs and the nerve ending in Plate II, figs. 19 and 20.

From these coils intra-epithelial fibres arise and can be seen in the reconstruction in Plate III, fig. 30, and also in part in the associated photomicrographs (Plate III, figs. 26 to 29). Two of these fibres were traced for a long distance through the epithelium and ended in the stratum corneum with bulbous swellings. One of these fibres (Plate III, fig. 27) in its course showed a number of varicose swellings, reminiscent of the swellings seen in the very earliest stages of axon cylinder degeneration. The second fibre (Plate III, fig. 29) is interrupted in the peripheral part of its course but can be traced as a dotted line to its termination in the stratum corneum, where it ends in a definite knob. The condition of these two fibres suggests that as the outer layers of the epithelium are shed, at the same time the peripheral portions of the intra-epithelial nerves undergo degeneration and may retain the faculty of forming new end-organs from the non-degenerated part, which then grows outside with the epithelial cells.

In Plate II, fig. 18, a second example of Type V_A can be seen. In a camera lucida reconstruction (not shown) of this and the adjoining sections the coil structure is clearly

brought out. From this coil an intra-epithelial fibre arises and terminates freely in the stratum corneum. Other intra-epithelial fibres, not seen in this photomicrograph, also arise from the coil.

CONCLUSION

Intra-epithelial nerve fibres arise from five sources: In the sheep fibres from only the first two of these sources were found; in the mole and mouse three; in rat and rabbit four; and in ferret and man five.

Intra-epithelial plexuses were observed in the mole and mouse for the first time.

In the human gum three new structures were seen in the papillæ: (1) An elongated club-like swelling containing a neurofibrillar network; (2) simple loops formed either from single or several fibres; (3) large coils containing neuro-fibrillar networks from which intra-epithelial fibres arose.

In sheep, ferret, and man, nerve fibres could be traced to the stratum corneum. In man the appearance of some of the fibres suggested the possibility that the most distal parts of the nerve fibres undergo degeneration simultaneously with the shedding of the surface cells of the epithelium.

EXPLANATION OF PLATES

All figures show photomicrographs with the exception of Pl. I, fig. 1 (drawing); Pl. II, fig. 20, and Pl. III, fig. 30 (camera lucida drawings).

PLATE I

- FIG. 1.—Drawing to illustrate the sources of the intra-epithelial nerve fibres:
 Type I: Individual fibres passing directly from a nerve bundle to the epithelium.
 II A: Individual fibres arising as in I but running along the border between epithelium and connective tissue for some distance before entering the former.
 II B: As in II A, but several fibres running together along the epithelial border, and entering separately into that tissue.
 III: Fibres arising from a sub-epithelial plexus.
 IV: Fibres arising from an intra-papillary plexus.
 V A: Several fibres arising from a large neuro-fibrillar coil.
 V B: Single fibres arising from a small close coil.
- FIG. 2.—Sheep: Intra-epithelial fibres. Note the wavy course of the fibres as they pass between the cells.
- FIG. 3.—Mole: Type II B fibres, some of which divide either before or after entering the epithelium and end freely or with knob-like swellings within the epithelium.
- FIG. 4.—Rabbit: Intra-epithelial fibres; one appears to end within an epithelial cell. There is a very distinct loop on the course of the other fibre.
- FIG. 5.—Mole: Various types of intra-epithelial fibres: (a) thin fibre with long wavy course and free nerve ending; (b) thick fibre ending in a rough elongated swelling; (c) thin fibre with knob-like ending; (d) willow-tree fibres.
- FIG. 6.—Mole: Merkel's discs.
- FIG. 7.—Mole: Intra-epithelial plexus.
- FIG. 8.—Rabbit: Type II B fibres.
- FIG. 9.—Rat: Type II B fibres.
- FIG. 10.—Rat: Higher magnification of epithelial process shown in fig. 9. Note loop-formation.

PLATE II

- FIG. 11.—Rat: Type III fibre with curious acute-angled course.
- FIG. 12.—Mouse: Type III fibre.
- FIG. 13.—Mouse: Type I fibres.
- FIG. 14.—Mouse: Intra-epithelial plexus.
- FIG. 15.—Ferret: Type V. The fibre terminates in a small bulbous swelling.
- FIG. 16.—Ferret: (a) portion of an intra-papillary coil not in focus; (b) intra-epithelial fibre traceable to under-surface of stratum corneum.
- FIG. 17.—Human: Type II A.
- FIG. 18.—Human: Type V A.
- FIG. 19.—Human: Intra-papillary nerve ending located at the apex of the papilla. It is an elongated club-like swelling, containing a neuro-fibrillar network.
- FIG. 20.—Camera lucida reconstruction of section shown in fig. 19 and the two adjacent serial sections.

PLATE III

- FIG. 21.—Human: Type I. The fibre ends in the stratum corneum.
- FIG. 22.—Human: Type III.
- FIG. 23.—Human: Single intra-papillary nerve fibre forming a loop.
- FIG. 24.—Human: Intra-papillary nerve loops.
- FIG. 25.—Human: Intra-epithelial fibre dividing a short distance before its termination into two branches which have bulbous endings.
- FIG. 26.—Human: Type V A. Almost the whole intra-epithelial course of the fibres can be seen.
- FIG. 27.—Higher magnification of fig. 26. One epithelial fibre with a few varicose swellings ends in the stratum corneum with a knob-like swelling.
- FIG. 28.—Human: Section adjacent to the one in fig. 26. At the tip of the papilla fibres containing neuro-fibrillar networks form a part of the intra-papillary coil.
- FIG. 29.—Alteration in focus of fig. 27. The fibre ends with a knob-like swelling within the stratum corneum. Near the stratum corneum the fibre forms a dotted line suggestive of degenerative changes. It is possible that the part of fibre proximal to this degeneration retains the faculty of forming a new ending.
- FIG. 30.—Camera lucida drawing of three consecutive serial sections including sections shown in figs. 26 and 28. Type V A.

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PLATE II



FIG. 11

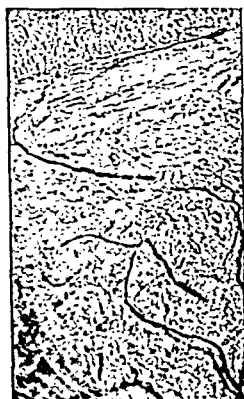


FIG. 12



FIG. 13



FIG. 14



FIG. 15



FIG. 16



FIG. 17



FIG. 18



FIG. 19



FIG. 20

PLATE III



FIG. 21



FIG. 22



FIG. 23



FIG. 24



FIG. 25



FIG. 26



FIG. 27



FIG. 28



FIG. 29



FIG. 30

Section of Medicine

President—T. IZOD BENNETT, M.D., F.R.C.P.

[November 27, 1945]

DISCUSSION ON THE STETHOSCOPE VERSUS X-RAYS

Dr. James Maxwell: The constant advances in medicine are placing an ever-increasing burden on the medical student. The tendency is to continue adding to the number of subjects which he has to study and the detail which he must absorb, and this process is beginning to place an intolerable burden upon his intellectual powers. The time has come when we should consider what must be retained and what may safely be discarded.

In the past the main emphasis in teaching lay on physical examination, and this had hardly altered for a century or more. The methods were those of Laennec and few fresh signs of value were described after his time. The advent of X-rays has added a method of examination which has greatly increased the accuracy of diagnosis. In fact X-rays are now essential in the recognition of all respiratory conditions.

Most doctors are apt to assume and, even worse, to announce to their patients that the failure to detect physical signs implies a healthy respiratory tract. Nothing could be further from the truth. This mistaken idea leads to the unfortunate result that disease of the lungs, and in particular tuberculosis and bronchial carcinoma, is almost certain to be missed at the very stage when treatment would stand a good chance of success.

The reason for this attitude on the part of the doctor must lie in his training. Many months are spent in drilling the student in physical signs, whereas chest radiology is hardly taught in many medical schools. It would appear that the object is to produce a clinician who is competent to reach a diagnosis so long as signs are present, but there is a failure to stress the fact that disease may exist without any abnormal physical findings. Of course it would be difficult to keep the student to the requisite pitch of keenness in the face of such an admission, for he would naturally wonder why he should spend so long learning physical signs when an X-ray must always be taken in order to be sure that something has not been missed. If chest X-rays were entirely reliable there would be something to be said for abandoning the teaching of physical signs, but in fact there is a small but definite percentage of error, even in well-taken films.

The standard postero-anterior film is a composite picture of the whole depth of the chest, and quite large lesions may sometimes fail to appear if they are situated far to the front or to the back. Also, a small lesion may be obscured by a rib or clavicle, and quite a large area of the lung field is hidden behind the heart and below the dome of the diaphragm. Early tuberculosis and early malignant disease may easily be missed, and bronchiectasis may be present without any radiological evidence. Multiple X-rays, which include the standard postero-anterior film and also antero-posterior and lateral views, yield far more information than can be obtained by the method in use at present and they are likely to be increasingly employed in the future. In some cases further evidence will be furnished by a bronchogram or tomogram when no abnormality has been seen on the plain film. In order to be quite certain that the chest is healthy we must therefore still depend upon the combination of physical examination and X-rays; and the teaching of the student must include both of these in their proper proportions.

When one comes to assess the physical signs which are of real value it becomes apparent that most is learnt from the correct interpretation of added sounds. Rhonchi and sibili indicate bronchitis or asthma, while râles reveal bronchiectasis or cavitation, and friction is diagnostic of a dry pleurisy which often leaves no trace on the X-ray. The chief emphasis in the teaching of physical signs should therefore be laid on added sounds. Inspection, palpation and percussion will still have their place, but their message is relatively simple to read and to interpret. Many of the older signs, Grocco's triangle and the rest, are of traditional value only and the time has come for them to be abandoned.

Should the reporting of the X-ray be done entirely by radiologists, or should the student be taught to read his own films? Undoubtedly the clinician, who is familiar with the physical condition of the patient, is in the best position to interpret chest X-rays, and it would seem right that the student should be taught this art at an early stage. This need not necessarily mean an increase on his already overloaded curriculum. His training should start in the departments of anatomy and physiology, where he should receive a thorough grounding in the radiological appearance of the normal chest. Good films, taken in all the standard positions, would be of far more use to him than much of the descriptive anatomy which is taught at present, and normal bronchograms would convey

a clear conception of the bronchial tree as it functions during life. With this basis, and with subsequent instruction in the interpretation of abnormal appearances, the X-ray film would soon convey a message which he would be in a position to understand.

Finally, there is the legal aspect to consider. Failure to advise an X-ray of the chest might be considered to be evidence of neglect in the investigation of a patient. Nowadays it would not be a good defence to show that a full and careful physical examination had been carried out, and this might well be a serious matter for the medical practitioner concerned.

Dr. Peter Kerley: The limits of the stethoscope have been reached but within those limits it is an efficient and indispensable instrument. If a competent physician finds added sounds in the chest it is unusual for radiological examination to be negative provided the proper technique has been used. Moreover auscultation can give decisive evidence of activity in a tuberculous lesion which radiologically appears to be completely healed.

Radiology of the chest is still in its early stages and in the near future we may regard our present standards as obsolete and our pictures as crude images. Most radiological errors are due to inadequate use of the method and reliance on a single film. Although we know that many lesions hidden in the mediastinum can be revealed by a lateral view and that lesions hidden by the ribs and breasts are shown by an antero-posterior view, yet such views are not adopted as routine procedure. Tomography which often throws immense light on unsuspected pathological changes is not used nearly enough.

It is true that many different diseases show what are apparently identical radiological appearances but if we can obtain increased detail and use new methods to delineate all the different structures in the chest, radiological diagnosis may approximate to that of the morbid anatomist. We know that the wave form from a condenser discharge unit is more suitable for chest work than that from a transformer and we know that we can get improved detail by using higher speeds and finer focus tubes. There is no real obstacle to the production of an X-ray set incorporating all these factors. Generally speaking the finest detail on a radiogram is equal in size to the focal spot of the tube. At the moment we are using tubes with focal spots of 1 and 2 mm. but foci of one-tenth of a millimetre capable of withstanding high loads at short speeds should appear during the next few years. The use of these new factors would not only greatly increase detail but would enable us to produce double and quadruple magnification of suspected areas. Some experimental work has already shown that we can differentiate the superficial and deep lymphatics in certain diseases, and we should soon be able to distinguish isolated tubercles from small end-on vessels.

In the examination of the heart X-rays lag far behind the stethoscope but if we consider the cardiovascular system as a whole there are a variety of pulmonary vascular X-ray appearances such as azotemia and impending failure which precede any clinical or stethoscopic findings by an appreciable interval. Cardiovascular radiology has been built up largely by cardiologists who have made great advances by fluoroscopy but screen examination is no substitute for radiography. The use of elaborate equipment and such new methods as angiocardiology should give a new impetus to the investigation of heart disease and might even relegate the stethoscope to a subsidiary position.

Dr. L. G. Blair: As has been shown by the previous speakers, radiology is superior to the examination by the stethoscope, or for that matter, to physical examination generally, in the investigation of the vast majority of chest conditions. In the first place, it is possible to show by X-rays, lesions which give no physical signs, because of the very nature of the lesion or because physical signs are masked by overlying emphysema.

Slides illustrating the very varied conditions in the chest which may give no physical signs were then shown as follows: Primary pulmonary tuberculosis. Early pulmonary tuberculosis. Cavity formation in pulmonary tuberculosis. Miliary tuberculosis. Single cysts. Pneumoconiosis. Secondary carcinoma. Secondary sarcoma. Primary tumour of lung. Hernia. Foreign body in œsophagus.

The speaker then continued

These cases, selected at random, are by no means all the conditions which may present radiologically, and yet show no clinical signs, but they are sufficiently varied to illustrate the very wide field in this group.

Secondly, there is the very large group where physical signs are present, but where, nevertheless, radiology is of considerable importance. It must be remembered that the physical signs found, such as diminished expansion, hyper-resonance or impairment of percussion, alterations in intensity or character of the breath sounds, alteration of voice conduction and the added sounds, merely indicate change in the underlying lung or pleura, such as the presence of fluid or air in the pleural cavity, of consolidation or collapse in the lung, of breaking-down of lung tissue, or of fibrosis; yet these pathological

conditions may be common to many of the diseases found in the chest. There are thus no physical signs of pulmonary tuberculosis, no physical signs of carcinoma, no physical signs of lung abscess, as the textbooks would suggest. The physical signs in all three conditions I have mentioned may be absolutely identical. The shadows caused by these conditions are, however, frequently diagnostic.

Thirdly, and again where physical signs are present, and the diagnosis beyond doubt, in the vast majority of cases the extent of the lesion is more accurately determined by X-ray examination.

To point the contrast of these large groups, and also to be absolutely fair, I would like to mention the comparatively few conditions in which there are physical signs present, and yet no radiological evidence of disease. The biggest group of these are the non-obstructive lesions of the bronchial tree, thus bronchitis may show little or nothing radiologically, and yet the physical signs of the condition may be extensive. There are certain cases of bronchiectasis which will show nothing in the straight X-ray, but the presence of persistent râles, particularly at the base, is suggestive of this condition. On the other hand, silent bronchiectasis may be demonstrated by radiography in the absence of physical signs. Tracheobronchitis, tuberculous or otherwise, frequently gives no radiological evidence of its presence but physical signs of themselves may suggest the diagnosis.

There is another condition where the physical signs are of paramount importance, and that is mediastinal emphysema. Crepitations synchronous with the heart beat, once heard will never be forgotten, and yet this condition as a rule gives no radiological appearances. I think, too, that dry pleurisy shows no evidence of its presence on the X-ray film.

Broadly speaking, in cardiac lesions, physical signs are ahead of X-ray examination, though of course, X-rays can be used to demonstrate alterations in shape and size of the cardiac silhouette. Dry pericarditis is, of course, a purely clinical diagnosis, but in the diagnosis of pericardial effusion, X-ray examination, and particularly screening, is often of supreme importance.

I have shown earlier that X-rays in the vast majority of cases help in the interpretation of abnormal physical signs, but occasionally, physical signs help in the differentiation of an opacity which may be due to fluid or to consolidation. Here, indeed, the physical signs may be of the greatest importance.

The activity or quiescence of a lesion, particularly a tuberculous lesion, is largely a matter for the clinician, from consideration of the history, and possibly physical signs. X-ray examination alone is unreliable.

This group where physical signs may be of paramount importance, is relatively very small. I would suggest, therefore, that in the investigation of chest disease, the present order of examination should be retained, namely, the taking of the history, the physical examination, followed by the X-ray examination. It should be remembered and taught, however, that in the diagnosis and treatment of chest conditions, the history is of supreme importance, radiology comes next, and that the physical signs are frequently only an aid to the correct interpretation of the shadows present on the X-ray film.

[February 19, 1946]

NUTRITIONAL NEUROPATHY IN REPATRIATED PRISONERS OF WAR FROM THE FAR EAST

Dr. C. Astley Clarke and Dr. I. B. Sneddon showed a film, taken at the Royal Naval Hospital, Sydney, illustrating the main clinical features of a nutritional neuropathy which had occurred in repatriated prisoners of war from Hong Kong. The men had been in captivity for over four years and their diet throughout had consisted largely of polished rice, the total nutritive value being only 1,600-1,700 calories daily. In addition the diet had been grossly defective in protein and the vitamin B complex. The neurological signs which developed in various combinations, usually within a few months of captivity, were optic atrophy, macular changes, nerve deafness and ataxia. In general, the ataxia was considered to be due to a peripheral neuritis but in some patients there was evidence of a cord lesion and the picture resembled subacute combined degeneration. One case showed a striking resemblance to amyotrophic lateral sclerosis.

Some patients developed fresh neurological signs while on an adequate parenteral intake of thiamin in the camp hospital. This was part of the evidence which Drs. Clarke and Sneddon brought forward in support of the theory that the neuropathy was not caused by a simple lack of vitamin B complex. In their opinion the syndrome was due to an anti-vitamin or toxic factor present in the rice which inactivated what little thiamin there was in the diet. The thiamin deficiency was rendered more severe owing to the low protein intake which prevented adequate bacterial synthesis in the gut.

The patients had shown little or no recovery since release from captivity in spite of massive vitamin therapy and a high calorie diet. It appears probable that after so long the changes in the nervous system are irreversible.

Dr. E. R. Cullinan: *An outbreak of beriberi in East Africa.*—In rice-eating communities it is usually accepted without question that beriberi results from living on polished rice from which the thiamin content has been removed. Similar outbreaks in various parts of the world among rice-eating communities who have lived on unpolished rice have usually been labelled epidemic dropsy, and thought to have been caused by a toxin. And yet a study of the descriptions of beriberi and epidemic dropsy suggests that the two syndromes are, at least clinically, identical.

The following episode may throw some light on the food aspect of this problem.

In a British garrison in East Africa during the month of March 1945 there was an outbreak among East African troops of a syndrome indistinguishable, except in a few minor and unimportant particulars, from beriberi. Mauritian and British troops in the garrison were unaffected. The syndrome was characterized by oedema of the legs, which was the presenting sign together with right-sided dilatation of the heart and peripheral neuritis. Other monosymptomatic evidence of malnutrition was consistently absent and the general physical state of the patients was good. All men of the garrison were examined by Kekwick, Watts, and myself, and we found 59 cases some of which were investigated in detail. We considered that the rice diet was at fault and on March 24 the diet was almost completely altered. From that time onwards the numbers of cases steadily lessened.

The staple article of food in the normal diet of East African troops is maize meal. In November 1944 it was found that the isolated position of the garrison and the fact that maize meal did not store well under the climatic conditions in the area, precluded the continued use of maize meal as the staple food. Nineteen ounces of rice were therefore substituted for the previous issues of fourteen ounces of maize meal and four ounces of rice. In February 1945 the stock of beans in the garrison was condemned because of high weevil infestation. During the months of January and February 1946 fresh vegetables were in short supply. By the middle of February the diet of the African native troops had thus considerably changed from the normal diet. The European and Mauritian troops were on a different scale. The main differences at this time between the food of the three races were first that the diet of the Mauritians and Europeans was considerably more varied and secondly that rice formed a much greater proportion in the African diet. The rice, which was lightly milled, was stored under good conditions in sacks. It was, however, old, and had on its surface contaminating spores and sporangio-phores of a variety of mucus. This variety of mucus has no known toxic properties to man. In its uncooked state the rice contained a theoretical sufficiency of thiamin and was active and adequate in relation to pigeons. The thiamin estimations were made by Titman.

After examining various possibilities it was found that while fresh lightly milled rice lost only 30% of thiamin in cooking, the suspected rice which was old and contaminated lost over 70%, and, moreover, produced beriberi in pigeons. It is possible that similar outbreaks may exhibit the same aetiological sequence of a toxin acting upon the thiamin and producing an epidemic of beriberi.

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Dr. J. D. Spillane: I think it might be useful to summarize the clinical features of the nutritional neuropathic syndromes which have been personally observed in prisoners of war of different nationalities during the past few years. It is not possible to provide an aetiological or pathological classification at present but we may discern at least six, fairly distinctive, clinical types of case. (1) Retrobulbar neuritis; (2) Polyneuritis; (3) Ataxic paraplegia; (4) Spastic paraplegia and quadriplegia; (5) Wernicke's encephalopathy; (6) Atypical encephalopathic states.

Other neurological symptoms and signs have been noted—anosmia, ageusia, trigeminal hypoaesthesia, tinnitus and nerve-deafness, nystagmus, diplopia, facial paresis, laryngeal paresis, urgency of micturition and dysaesthesiae of the lower limbs. In a few cases there has been intellectual deterioration.

Retrobulbar neuritis.—This has been common in German and Italian P.O.W.s in the Middle East and in Allied prisoners from the Far East. I have not seen it in German prisoners in this country nor in Allied prisoners from Europe. The condition may be acute or chronic and the eye has not usually suffered other detectable alteration. It appears to be self-limited; vision is rarely worse than 6/60. A few men from the Far East developed acute corneal opacification.

Retrobulbar neuritis may exist alone but it has often been associated with wet or dry beriberi or with the ataxic or spastic forms of paraplegia.

Polyneuritis.—I have not seen polyneuritis in British prisoners from Europe but it was present in some of the German cases from the Channel Isles. It was rare among the Germans and Italians in the Middle East but was very common among Polish refugees from Russia. It was, of course, also very common among prisoners from the Far East among which group the wet and cardiac forms of beriberi and famine oedema occurred.

Ataxic paraplegia.—We first saw this type of disability among the Germans and Italians in the Middle East P.O.W. camps but it has also occurred in Allied prisoners from the Far East. Painful dysaesthesiae of the feet and lower limbs usually preceded disturbance of gait. The latter frequently became grossly defective owing to loss of postural sensibility in the legs. Superficial sensibility was less affected, muscular power was good and the tendon reflexes remained brisk; plantar reflexes were flexor. This type of case was almost always associated with retrobulbar neuritis or some other cranial nerve disturbance.

Spastic paraplegia and quadriplegia.—I have seen this affection only in seven British P.O.W.s from the Far East. There was isolated, but gross, pyramidal disturbance chiefly affecting the lower limbs. The onset was acute, with cerebral signs such as confusion, amnesia, diplopia, loss of vision and generalized rigidity. Those that recovered were left with marked rigidity of the lower limbs, clonus, extensor plantar reflexes and absent abdominal reflexes. There was no sensory loss. I saw a few cases of lathyrism in Syria and but for the history of cerebral disturbance they were identical with these P.O.W. patients. None of the prisoners had apparently eaten any wild herbs or had access to any toxic substance.

Wernicke's encephalopathy.—Only one of the German Middle East cases developed this syndrome and following relief of the stupor and ophthalmoplegia with parenteral thiamin he developed, or more likely was left with, retrobulbar neuritis, deafness and ataxia. Wernicke's syndrome was sometimes seen as a terminal phenomenon in the Polish cases in the Middle East who had polyneuritis aggravated by infective illnesses such as dysentery, typhoid or malaria. I think mild cases of this encephalopathy recovered. I understand they were also seen in Far East P.O.W. camps.

Atypical encephalopathic states.—In a few Italian prisoners with dysentery or typhoid in the Middle East I have seen conditions of stupor, confusion, delirium, even mania, with tetanic spasms of the body, fibrillation, hyperactive tendon reflexes and grasping and sometimes sucking reflexes. The fiery red tongue of nicotinic acid deficiency was not present and in these and somewhat similar cases among Germans from the Channel Isles I have hesitated to call nicotinic acid deficiency encephalopathy. The Germans were suffering from severe diarrhoea and most of them were stained yellow from over-consumption of wild herbs. Many had polyneuritis. I do not think dehydration alone was responsible for these features. Hydration therapy sometimes failed whereas administration of milk, eggs, yeast, liver and vitamin B complex preparations gave satisfactory results.

Ætiology.—I have discussed elsewhere the ætiology of some of these syndromes and suffice it to say here that in none of them has it been clearly shown that they result solely from deficiency of one or more vitamins. The deficiencies which these men suffered were undoubtedly multiple but there is good evidence to suspect lack of some part of the vitamin B complex in the majority of these clinical affections. If such is the case it remains to be seen whether the neurological lesions are a direct result of such deficiency or whether the mechanism is more obscure. I have been impressed by the importance of dysentery and diarrhoea in this respect and we may have to look farther than the vitamins—to disturbance of carbohydrate, fat and protein metabolism and to the essential amino-acids.

But at any rate these observations on the nutritional disorders of malnutrition may focus attention on the metabolic aspects of other obscure disorders of the nervous system which are so common in this country. It is significant that subacute combined degeneration of the spinal cord is one of the few degenerative diseases of the nervous system about which something is known of its ætiology.

Major Brian H. Kirman, R.A.M.C.: I should like to make the following points about those released prisoners who passed through India:

Incidence of psychoses.—There were very few cases of psychosis. Some of the prisoners may at some stage in their captivity have developed Wernicke's encephalopathy and acute confusional states associated with nicotinic acid deficiency as suggested by previous speakers, but if so they had either got better or died before the capitulation of the Japanese forces, since no cases of these syndromes were recognized among patients coming to the hospital town, Jalahalli. The number of psychotics among the population at risk

was no greater than might have been expected had the diet been adequate in all respects. There were no special features about the psychoses which were similar to those encountered in any such group with the same age distribution.

Incidence of pellagra.—There were no cases of pellagra among the psychotics admitted to hospital town and pellagrous features were rare among general medical cases. Neither the mental nor the cutaneous features of pellagra were encountered and a typically pellagrous tongue was exceptional.

Cause of amblyopia.—A number of psychotics who had recovered sufficiently to be able to give a coherent history stated, as did many of the non-psychotic patients, that they had suffered from a sudden attack of amblyopia, in many cases some six months after the beginning of their imprisonment. In many instances it appears that a group of some half-dozen men were affected at the same time. Following the initial, acute attack, frequently with almost complete blindness there appears to have been a tendency to gradual improvement, with or without treatment by vitamin concentrates. In view of this history I would suggest that there is a strong probability that a toxic factor was operative in causing the amblyopia in addition to dietetic deficiency. There are a number of possible sources of such a toxin which could upset the already delicate metabolic balance in these grossly undernourished men. All manner of unusual articles were added to their diet or were smoked in lieu of tobacco. Some which were brought to my notice were, hibiscus, chrysanthemum and mulberry leaves, also cats, snakes, frogs and silkworms. A great variety of wild leaves and fruits were consumed at different times. It is possible that any of these may have contained a toxin which, though relatively harmless to the adequately nourished individual may have been sufficient to have caused amblyopia in the debilitated prisoner of war.

[March 26, 1946]

MEETING HELD AT MIDDLESEX HOSPITAL, LONDON

Disorders of the Sympathetic Nervous System [*Abstract*]

By A. LAPORTE, M.D.

Médecin des Hôpitaux de Paris

DR. LAPORTE took as his subject certain disorders of the sympathetic nervous system, dealing principally with:

- (1) Influence of the sympathetic nervous system in infectious diseases.
- (2) Influence of the sympathetic nervous system on the kidney, particularly in the production of nephritis and in the treatment of suppression of urine.
- (3) The sympathetic nervous system and the treatment of such conditions as angina pectoris, Raynaud's phenomenon, Buerger's disease, œsophageal spasm, &c.
- (4) The technique of choice for the injection of the stellate ganglion and splanchnic nerve.

The first and second sections dealt largely with the experimental work of which much has been due to the inspiration and perseverance of Dr. J. Reilly (and to whom Dr. Laporte held that the greatest credit should be given), Pathologist to the Hôpital Claude Bernard, Paris. In this work Dr. Reilly has had the close collaboration, on the clinical side, of Dr. Laporte during many years. The speaker called attention to a number of startling experiments, such as those in which the intestinal and mesenteric lesions of typhoid can be produced in a very short time by the application of a dilute emulsion of typhoid toxin to the splanchnic nerve, and those in which classical typhoid catatonia can be reproduced in dogs by washing the third ventricle with a very dilute solution of typhoid toxin. Not less interesting were his accounts, illustrated by microscopic sections, showing the effects on the kidneys of nocive stimuli applied to the pharyngeal mucous membrane in animals, effects which fail to appear if the splanchnic nerves have previously been divided.

Dr. Laporte has obtained many favourable results in prolonged angina pectoris, even in cases where the cardiac muscle has been seriously damaged; he has also had many good results in cases of Raynaud's disease, intermittent claudication, and in not a few examples of acute suppression of urine.

He illustrated the technique which has been found most satisfactory and emphasized that, in the case of infiltration of the stellate ganglion with novocain, the technique perfected by Dr. de Seze is so simple that it can be safely and successfully employed by a general practitioner or even a senior student.

The speaker paid tribute to the wonderful work achieved by R. Leriche and his school, and by certain workers in Marseilles.

Section of Laryngology

President—G. EWART MARTIN, F.R.C.S.Ed.

[February 1, 1946]

(1) Squamous-celled Carcinoma of Left Cheek Treated by Operation; (2) Squamous-celled Carcinoma of Left Tonsil.—NORMAN PATTERSON.

The first of these cases was that of a man aged 76. He was seen at London Hospital in 1926 with squamous-celled carcinoma of left cheek previously treated by Mr. Morris on two occasions by diathermy. Operation was carried out on December 29, 1926, by flap method as described by the exhibitor in *British Journal of Surgery* (1937, 25, 330). Recurrence took place in 1943 at old site but also involved the lower jaw. Operation was carried out again by means of flap method, September 3, 1943, at Royal Bucks Hospital. Later bony sequestrum separated. Mr. Patterson showed drawings illustrating the method which he had devised many years ago. He added that the condition was commoner in men than in women, but in his short series there were more women than men (4 men and 6 women).

For the case-history in the second male patient, aged 68, he was indebted to Mr. Robert D. Owen who referred the case to him for treatment. Secondary glands on the affected side were removed at the London Hospital by block dissection in March 1926. Three weeks later diathermy excision of squamous-celled carcinoma of left tonsil, anterior pillar, and base of tongue was carried out.

Both these cases were well, after twenty years.

The President said that formerly dissection was practised in his hospital, but now practically all the cases had been handed over to the radiologist for deep X-rays.

A. J. M. Wright said that in Bristol they were not accustomed to send all these cases to the radiologist. If he himself had a carcinoma in the cheek he would not have the slightest hesitation in choosing somebody to deal with it by diathermy rather than by radiation.

E. D. D. Davis said that it had been his experience that these tumours, treated by means of deep X-rays, died from secondary growths within eighteen months. Personally he preferred diathermy.

Mixed Salivary Gland Tumour in Palate.—R. R. SIMPSON.

F. B., male, aged 38.

September 1945: Swelling right parotid, size of an orange, and swelling of right half of palate, size of a tangerine orange. Palatal swelling bulges forwards and downwards and beyond mid-line causing some difficulty in chewing and swallowing.

Both swellings considered to be part of same tumour and of the mixed salivary type.

Mr. Simpson said that this large tumour had been present for several years. He first saw the patient in 1938, when the tumour was about half its present size. Should the tumour be treated by operation or should it be left entirely alone?

C. P. Wilson said that he did not think there was any doubt but that such cases were malignant. The consensus of opinion was that they were low-grade carcinomata.

If the tumour in the palate was causing trouble there was no reason why it should not be excised. The most satisfactory treatment seemed to be to treat these tumours with radiotherapy and excise them afterwards.

About a year ago he showed a patient in whom a tumour of this type in the peritonsillar region had been excised in 1922. Since that time he had had two or three further tumours in the parotid with recurrences, and had had excision and several courses of radiotherapy. Three years ago he developed a swelling of the ilium, which on exploration was also found to be of the same pathology. The patient was still working after twenty-four years, although he had a facial palsy on the affected side, and would probably show a further recurrence later.

Musgrave Woodman said that the principle which should be followed was to remove these tumours whenever they could be removed. He was certain that they were malignant.

although the malignancy was of low grade. They could be safely removed from the palate. When they occurred in the parotid it was wiser to leave them alone. He thought that they did recede to a certain extent under radium and X-rays. One patient whom he saw was a commercial traveller who had a large tumour which had been under observation for ten years. He did not want an operation because he was afraid that it would damage his voice and so handicap him in his business. He was treated by means of X-rays. He was still alive, but the tumour was rather larger than formerly though it had not increased to any great extent.

E. D. D. Davis said that in his experience X-ray and radium treatment had no beneficial effect on these tumours. It made a subsequent dissection operation much more difficult.

Boeck's Sarcoidosis with Nasal Lesion.—**F. C. W. Capps and J. C. Hogg.**

Male, aged 21. August 1945 attended King George's Hospital, Ilford, with a history of nasal obstruction for eighteen months, swelling of cervical glands, and an intermittent swelling of proximal phalanx of right middle finger. There was nodular infiltration of the nasal mucosa, redness and dryness of the pharynx, and many discrete rubbery glands on both sides of the neck. W.R. and Kahn were negative. W.B.C. 11,400 per c.mm.

X-ray of finger: "Upper half of medullary cavity has lost its outline when compared with other phalanges."

Histology of the nasal lesion: A fibrolympho-angioma was suggested, but the pathologist admitted that he had seen nothing like it before. A section was stained for tubercle bacilli, but none was found.

In December 1945 the patient was seen at St. Bartholomew's Hospital. Clinical picture was substantially the same, but enlarged glands were also found in the left axilla. There was no enlargement of the spleen, and there were no inguinal glands. The radiograph of the chest showed increased hilar shadows suggesting glandular enlargement. Boeck's sarcoidosis was diagnosed. Nodule from nose was inoculated into a guinea-pig, but the guinea-pig unfortunately died of pneumonia the day following. Gland was removed for section and the report was: "Node almost entirely replaced by a mass of pathological tubercles packed closely together. Giant cells are very sparse, but fibrosis is considerable. A few areas of early hyaline degeneration but no caseation. No tubercle bacilli seen."

The histological picture strongly favoured a diagnosis of Boeck's sarcoidosis. The patient was fit and well and there were no other obvious lesions in the upper respiratory tract. The tonsils had been removed.

This was shown as a rare condition of which not many cases were seen. There was some doubt as to the diagnosis at first, but it had been confirmed on histological grounds. There was strong presumptive evidence of sarcoidosis. Mr. Hogg asked for suggestions as to any form of treatment which might improve the condition. The patient had a very poor airway, and it was of this he chiefly complained.

E. D. D. Davis said that clinically this condition looked like a tuberculoma, but Mr. Hogg had told them there was no ulceration. The nodules did not break down and ulcerate. Lupus was a very chronic disease and continued for many years. The section had a different appearance from that found in common lupus.

J. H. Otty said that a number of these cases were seen up North but he looked upon this as a case of tuberculoma of the nasal mucosa and these cases, as a rule, did not ulcerate. He did not think he had seen lupus within the nose without lupus of the cheek or elsewhere in the skin of the face. He had treated them with light diathermy.

Tumour of Nasal Septum (Chondrosarcoma). Operation and Recurrence.—**ROBERT D. OWEN.**

H. J. W., male, aged 43. First seen in September 1943, when he complained of complete nasal obstruction of long standing. Examination showed a red smooth mass arising from the nasal septum and causing complete occlusion of both posterior nares. X-rays showed the right antrum diffusely opaque, with a rounded opacity extending into the left antrum. An exploratory operation was performed, with right lateral rhinotomy approach, and the whole of the nasal septum, with the mass, was removed. The pathological report showed the mass to be composed mainly of chondromatous tissue, but suggestive of chondrosarcoma. In November 1944 another operation was performed for a recurrence involving the floor of the right frontal sinus, extending down to the inner canthus, also in the roof of the mouth in the mid-line. Further sections showed a similar chondromatous structure. It was difficult to judge the malignancy on histological grounds, but the tumour was evidently forming metastases. Opinion varied as to whether any response could be produced by teloradium, and the problem was how far further surgical interference could be carried out. The man's present condition showed further recurrences, particularly in both orbits.

The pathological report showed that two of the sections, namely, those of tissue from the canine fossa and from the left ethmoidal region, consisted mainly of chondromatous tissue. It was difficult to decide from the histological appearance whether it was a simple recurrent chondroma or a chondrosarcoma, but from the way it appeared to be

destroying the tissues it was probably the latter. Another section, probably fibrous tissue from the antrum, showed, in one part of it, some chondromatous infiltration. The tumour was avascular. He asked for suggestions from the Section as to whether surgery was the best line of treatment or whether radiation in one form or another could be introduced.

Gavin Young said that he had at the moment two of these cases. He was assured by the radiotherapist that they were not radio-sensitive, and it had been customary to deal with recurrences as they occurred, by diathermy.

Chondroma.—W. STIRK ADAMS.

A man, aged 22, in September 1933 came under the care of Mr. Holt Diggle at the Christie Hospital, Manchester, suffering from a swelling in the left side of the face, which on surgical exposure proved to be an ossifying chondroma with no evidence of malignancy. The tumour was excised and radium inserted into the cavity of the antrum. From then he remained well until October 1936, when a left orbital swelling occurred, but subsided. This returned in 1938 and, in November, an external operation was carried out for removal of the tumour. Three years later he was referred to Mr. Stirk Adams. At this time there was a firm fullness in his left cheek and inspection of his nasal cavity showed a mass which had extended through the nasal septum and was pressing on the lateral nasal wall on the right side. A sub-labial excision of the mass was undertaken and he remained well until March 1943, when a further operation was carried out because of increasing trismus. The neoplasm had by this time extended posteriorly into the sphenomaxillary fossa. A further partial removal was carried out in the following November, in an attempt to relieve his spasm, and at this time the mass was found to have extended into the basi-occiput and the basi-sphenoid. In April and October 1943, courses of deep X-rays were attempted but could not be tolerated. Biopsy material removed at operations was examined and in every case Professor Haswell Wilson reported a simple chondroma with no evidence of malignancy. The prominent symptom, apart from that of the local lesion was a devastating continuous pain in his face and head, and several of the operations were carried out because, after operation, he obtained relief from this pain for weeks or months. The last attempt to relieve him was carried out in May 1944. He died of increasing weakness but without evidence of somatic secondaries, in November 1944, eleven years after his first symptom.

It was unwise, therefore, to regard any chondroma developing in the nasal capsule as innocent.

Lionel Colledge considered it very unlikely that the tumour was radio-sensitive. He thought it most undesirable to make incisions in the face, they were disfiguring, and they were not necessary from the point of view of obtaining increased exposure. The customary procedure in what was called Rouge's operation gave all the exposure required.

Laryngeal Granuloma following Intratracheal Anæsthesia.—IAN G. ROBIN.

Woman, aged 50. Two years ago she had two gynaecological operations both under an anæsthetic. She complained of hoarseness immediately afterwards and ever since. He brought forward the case rather as a supplement to the Presidential Address (Ewart Martin, *J. Laryng.*, in press). Three months ago there was definite granuloma. He thought there was now a small granuloma on the other side, perhaps due to a recent attack of influenza.

The President said that he had seen three further cases since those previously reported by him. One of these very much resembled the present case. It was difficult to see why a tube passing into the larynx could give rise to a granuloma in one case and not in hundreds of others.

I. Simson Hall said that the number of cases of this form of laryngeal irritation seen was extremely small when the large number of anæsthetics carried out every day in all parts of the country was considered. He suggested that there must be some predisposing cause apart from the trauma of passing the tube. As a possible suggestion of this causation it was noteworthy that fibroma or granuloma of the cord was most liable to form when the voice was used excessively in the presence of slight inflammation. It was possible that slight laryngeal inflammation or slight cold might be a predisposing cause of the granuloma formation following intubation.

C. P. Wilson said that he had seen a case in which a granuloma of the larynx had occurred as a result of an intratracheal tube having been left in the larynx for a week. The nurse in charge of the patient had removed the metal connexion of the tube from the nose without realizing that it was attached to the intratracheal rubber tube. The patient had complained of no discomfort other than loss of voice, and it was not until the surgeon had gone down to the country and examined the patient a week later, that it was discovered that the tube was still in position. In this case the granuloma must have been due to trauma.

J. H. Otty said that he had only seen one such case in Aberdeen in the last fifteen years. He supported Mr. Hall's contention that infection might play a part as the only case in Aberdeen followed a bronchoscopy for bronchiectasis.

R. D. Owen said that he thought the practice of passing the tube down blindly under pentothal anæsthesia only, was to be deprecated.

[March 1, 1946]

DISCUSSION ON IDIOPATHIC RECURRENT LARYNGEAL NERVE PALSIES

Maxwell Ellis: The terms of reference restrict this discussion to about one-quarter to one-third of all cases of recurrent laryngeal nerve paralysis—a figure common to a number of statistical surveys of which the more recent are by New and Childrey (1932), Smith, Lambert and Wallace (1933), Work (1941) and Suchs (1943). The cases represented are drawn from widely different areas in America and Britain, and this agreement in incidence of a disease of unknown aetiology is remarkable and may indicate the constant presence and effect of some unknown, or unsuspected, disease process. The absence of any gross or demonstrable lesion has stimulated speculation. The most popular conception ascribes the condition to an insidious invasive peripheral neuritis secondary to some circulating toxin, or to a vitamin deficiency, or to rapid change in temperature. I fancy that glandular dyscrasia and allergy could be added without fear of contradiction. However, it is fair to mention that Alcantaro and de Ocampo (1939) investigated the larynges of 37 infants suffering from beri-beri and found in 31 cases a partial or complete paralysis of a vocal cord. They believe that irritation of the recurrent laryngeal nerve occurred, followed by degeneration, and dismissed the possibility that pressure on the nerve due to the associated cardiac enlargement might have been responsible. These laryngeal findings are extraordinary, and have been seen recently in returned prisoners of war suffering from nutritional disorders. A few cases occurring during acute infections and after direct exposure of the neck to cold are recorded, but in the bulk of cases no such history is obtainable.

Males are affected nearly twice as frequently as females, and the left cord nearly twice as often as the right. Both cords are involved in only 10% of cases, or even less. The first and second of these observations could lend some support to peripheral neuritis as a cause, since males are more likely to undergo exposure to both weather and infection, and the left recurrent nerve from its greater length is more vulnerable to adjacent disease. But, when all is said, the mere presence in this group of any case proclaims failure in discovering a precursory incident of aetiological significance.

SYMPTOMS

Hoarseness or a weak voice are the usual symptoms for which the patient seeks advice, and choking or coughing attacks may occur on deglutition. Routine post-thyroidectomy laryngoscopic examination has shown that one-third of all cases of unilateral paralysis following the operation are symptomless. It therefore is likely that a number of idiopathic unilateral cases never come for examination and consequently are not recorded. Bilateral paralysis is usually accompanied by dyspnoea on exertion, or even at rest, and sometimes by stridor. This gradation in symptoms of impaired respiratory movements is a function both of the general build and occupation of the patient, and of the relative position of the vocal cords. The former needs no special description, and the latter has probably received overmuch since the paper published by Semon in 1881. The size of the glottic chink is the all-important and vital factor in prognosis.

PROGNOSIS AND TREATMENT

Unilateral paralysis occasionally recovers spontaneously, but in any case the disability is slight, the prognosis therefore good, and treatment unnecessary. Bilateral paralysis seldom undergoes a natural resolution, and it is the chief concern of the practical laryngologist, as fatal asphyxia may at any moment supervene. Prognosis, at the best, is uncertain, and, at the worst, disastrous. These cases are rarely of rapid onset, but they then present no problem as immediate tracheotomy is imperative. When the onset is slower, hasty action is unnecessary, but early decision is desirable if the patient is to return to anything like a normal existence. For many years these cases have been treated by permanent tracheotomy, but such a permanent fistula has certain obvious disadvantages, although when properly constructed low down in the neck and properly managed it need cause only minimal discomfort. However, the patient almost invariably will exert the maximum pressure to rid himself of this disfigurement. Earlier surgical approaches to the problem were first to restore function by nerve anastomosis, and secondly to restore airway by excision of some of the apposed soft tissues. Nerve anastomosis, usually joining the recurrent laryngeal to the descendens hypoglossi, has not proved entirely satisfactory, as in late cases fixation of the crico-arytenoid joint and atrophied muscles are present. Excision of portions of the true and false vocal cords was nearly always followed by the growth of obstructive scar tissue. Following this same principle, Hoover (1932) performed a submucous resection of the vocal cords and soft tissues of the larynx,

hoping to secure adhesion of the mucosa to the internal surface of the thyroid cartilage by firm packing. This procedure has not been altogether successful. Kelly (1941) has introduced a new principle by excising the arytenoid cartilage through a transthyroid approach, hoping (a) that the tension of the vocal cord would disappear, allowing it to fall away from the mid-line, (b) that the respiratory space left posteriorly by removal of the cartilage and atrophy of the cut muscles would be obliterated by scar tissue and remain permanent, and (c) that the position of the anterior third of the cord would be relatively unaltered, preserving a serviceable voice. He has performed this operation on a number of cases and finds that the result is functionally satisfactory. This orthopedic principle was adapted from another introduced by King (1939 and 1940), who began by performing an arthroplasty of the crico-arytenoid joint combined with a tendon transplant (using the anterior belly of the omo-hyoid), and ended by discarding the transplant and creating an arthrodesis of the joint with the arytenoid fixed in abduction and external rotation. The approach is posterior after dividing most of the attachment of the inferior constrictor muscle to the posterior border of the thyroid ala. The posterior crico-arytenoid muscle is divided at its insertion into the base of the muscular process of the arytenoid, the crico-arytenoid joint is opened widely, and the arytenoid freed from the fibres of the interarytenoid muscle along its posterior border and body, and from those of the lateral crico-arytenoid along the anterior border. The vocal process is then encircled by a catgut suture which is drawn through the lamina of the thyroid cartilage and tied so that the arytenoid is fixed in abduction and external rotation. King found by experience that the best result was obtained by operating on only one side, but if there is insufficient airway the other side should be treated likewise. He also found that patients can both open and close the vocal cords, although the larger range of movement develops on the unoperated side. The cord on this side will frequently pass across the mid-line in phonation. He considers that these movements are due to the action of the cricothyroid muscles in increasing the antero-posterior diameter of the larynx, drawing the cords towards the mid-line.

Most of the experience gained in treating bilateral recurrent nerve paralysis has been on cases following injury to the nerve, generally during thyroidectomy, as bilateral idiopathic paralysis is uncommon, but there is no reason why the same principles should not apply. My only personal experience of the Kelly and King operations has been on the cadaver, but the technique is not essentially difficult although one must be prepared to be painstaking in defining anatomical landmarks clearly, and in the precise placing of the anchoring sutures.

SUMMARY

In idiopathic recurrent laryngeal nerve palsies no cause has yet been discovered, but peripheral neuritis is a possibility. Unilateral cases are accompanied by few symptoms, are of reasonably good prognosis, and require no treatment. Bilateral cases are uncommon and always require some form of surgical treatment, of which permanent tracheotomy is the simplest. Recently operations on the arytenoid cartilage and crico-arytenoid joint have been devised, which are rational in conception, not especially formidable in technique, and reasonably successful in outcome.

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Macdonald Critchley: Perhaps I can best contribute to the symposium by discussing the phenomenon known as Semon's law and in particular its possible explanation.

In the German edition of Morell Mackenzie's textbook—translated and edited by Felix Semon—we find the following footnote: ". . . in many cases in which central or peripheral lesions unquestionably affect the whole nerve (most frequently in cases of pressure upon the entire trunk of the recurrent laryngeal nerve in cases of aneurysm of the aorta) the symptoms of paralysis of glottis-openers only are seen during life. . . . This proclivity of the fibres going to the abductors to be affected exclusively or long before the others, is very strange."

It was indeed strange and quite unexpected. But Semon had noted it in a series of his own patients and had reported it at the Clinical Society of London in 1878. By 1881 he had been moved to publish in the newly appearing *Archives of Laryngology*, a paper—now a classic—under the elaborate title "Clinical remarks on the proclivity of the abductor fibres of the recurrent laryngeal nerve, to become affected sooner than the

adductor fibres, or even exclusively, in cases of undoubted central or peripheral injury or disease of the roots or trunks of the pneumogastric, spinal accessory, or recurrent nerves".

But unfortunately he had been forestalled a few months before by Rosenbach, who upon the basis of a solitary case of carcinoma of the œsophagus had stated "... in compression of the trunk of the recurrent, the function of the abductors suffers first, and that of the adductors is implicated only later on".

The eponymous term Semon's Law has rightly passed into medical terminology, though some Continental sticklers may continue to speak of the Rosenbach-Semon law, or even the Gerhardt-Rosenbach-Semon law.

With the passage of sixty years it is not surprising that cases should occasionally be reported which show themselves (or appear to) as exceptions to this law. Perhaps it is a matter for wonder that the exceptions have been so few. But for this reason some—like the Chevalier Jacksons—would prefer to speak of Semon's rule rather than Semon's law, a distinction which might be regarded as a quibble.

Perhaps the majority of those exceptions comprise pseudobulbar laryngeal palsies, due to supranuclear lesions. This at least is what Semon afterwards affirmed, namely in 1913, when he emphasized that his law only concerned the laryngeal nerves from the nucleus downwards. Semon must, however, bear some of the blame for this misconception, for all his early papers on the subject referred to both peripheral and central lesions. By "central" Semon probably meant "nuclear" lesions, though most present-day neurologists might well assume these to refer to supranuclear locations.

Anyway the point is a good one, and the fact remains, I think, that supranuclear affections of the nucleus ambiguous do not necessarily behave according to Semon's law, e.g. in cases of pseudobulbar and progressive spastic bulbar paralysis, as shown by Collier, Critchley and Kubik, and others.

Later authors have read more into the law than Semon originally stated in that it is now taught that with progressive affections of the recurrent laryngeal nerve, the abductors are the first to be affected, while the tensors of the cords are implicated later, and the adductors last of all. Or, in terms of the muscles involved, the crico-arytenoideus posticus suffers first, then the thyro-arytenoideus, and lastly the crico-arytenoideus lateralis. The arytenoideus, having a bilateral nerve supply, is not affected in unilateral cases, while in bilateral disease it is affected very late.

Experimental physiologists have since shown that the law holds true for processes other than pressure effects or disease. Thus the abductor components of the recurrent laryngeal nerve have proved to be more sensitive than the adductor elements to such influences as drying (Risien Russell) and to freezing (Gad and Fränkel).

The many and diverse views that have at various times been proposed to explain Semon's law may best be arranged in chronological order.

Muscular hypotheses.—(a) Abductor group requires a greater volume of blood (Clausberg). (b) Abductors differ in chronaxy from the adductors (Tarneaud). (c) Abductors early lose their excitability after death (Jeanselme and Lermoyez). (d) Adductors are mechanically better placed than the abductors (Gowers). (e) Abductors suffer because the nutrient artery is involved (Robinson).

Location of abductor fibres within the recurrens.—A more peripheral siting of the abductor fibres suggested (M. Mackenzie)

Double innervation of adductor group.—(a) From spinal components (Tissier). (b) From superior laryngeal nerve (Cohen Tervaert).

Abductor paresis is really an irritative adductor spasm or adductor contracture (Krause). *Glottis-closure is subserved by a powerful cortical centre* (Bosworth; Risien Russell; Horsley).

Abductor proclivity is an instance of a general axiom that extensors are more vulnerable than flexors (Ferrier).

Glottis-closure is phylogenetically an older function of the larynx than is the opening of the glottis (Negus).

Some of the foregoing suggestions can be disposed of quickly.

Morell Mackenzie's original idea was that the abductor fibres were disposed peripherally in the recurrens and were therefore sensitive to pressure. But Risien Russell later showed that the abductor filaments lie mesially and the adductor filaments laterally.

The theory of double innervation is a plausible one but is not supported by anatomy, though bilateral innervation of the arytenoideus is of course a factor which may assist in maintaining closure of the glottis in unilateral lesions of the larynx. The fact that Semon's law applies to lesions of the vagus as well as the recurrent, and its occurrence in bilateral lesions of the larynx, are points against the theory of double (or bilateral) innervation.

Spasm of adduction (rather than weakness of abduction) is a not unnatural suggestion, and was at one time entertained by Semon himself. But subsequent experience rendered this idea unlikely, (1) because the adductive process was observed at times to continue for years—far longer than nerve-irritation was likely; and (2) because dissection of the laryngeal muscles confirmed a greater degeneration in the abductor set. Krause's theory of primary neuropathic contracture of the adductor muscles was the basis of another prolonged controversy, and here again Semon was able to point out that when laryngeal palsies accompanied multiple palsies elsewhere in the body, loss of power, and not contracture, was the rule.

The role of the cortex was regarded as a possible explanation, and, supported by most careful experimental work by Risien Russell, Horsley and Semon himself, has never been really put out of court. It ties up with the older conception of the dual role of the larynx, the adductive elements being connected with phonation and the abductive elements with respiration. The former was found to have considerable representation in the cerebral cortex, the latter having mainly a medullary hierarchy—though the circumstances differed slightly according to the kind and age of the animal studied.

Much attention has been paid to the idea that Semon's law is merely part of what might be called Ferrier's law, which states that in neurological disease the extensors of the limbs are always affected more than the flexors. It was imagined that the limb-extensors correspond with the laryngeal abductors, and the flexors with the adductors. Semon, however, pointed out that to invoke a general law of extensor vulnerability was merely to re-state the problem and simply to postpone the explanation. (Indeed the correctness of Ferrier's law is open today to serious doubt.) Semon made the point that both flexor and extensors of, say, the lower limb subserve the same functions of posture and of progression, while the adductors and abductors of the larynx serve two separate and distinct functions, namely phonation and respiration. Secondly abductor palsy is characteristic of organic disease and adductor palsy of hysteria; whereas no such selectivity occurs between functional and organic paralysis of a limb. Lastly Risien Russell had found that after division of the adductor filaments of both recurrences, stimulation of the cortex would not produce any inhibition of the abductors, such as would be expected to occur in the case of true antagonistic muscles.

The brilliant researches of Negus have afforded what is so far the most satisfying solution to the problem of Semon's law. Far from subserving two functions as Semon taught, the larynx according to Negus, has several, of which the most primitive is that of shutting-off the air passages from the gullet. For this purpose a sphincteric muscle at the entry of the larynx was developed, the homologue of the adductor group. Both phylogenetically an ontogenetically the glottis-closers are the oldest structures in the larynx and presumably therefore are more resistant than structures of later appearance and development.

Today this is perhaps the most plausible way of accounting for Semon's law, though one must admit that as an hypothesis it is not completely satisfying. The sphincteric conception of the larynx is perhaps an over-simplification. Most sphincters—if not all—are endowed with a sympathetic as well as parasympathetic innervation, which is not the case in the larynx. Furthermore, the interpolation of the arytenoid cartilages, and the division of the larynx into upper and lower compartments detract from the idea of a simple valve-like or sphincteric action.

Nevertheless it is not unfair to regard the larynx as being made up of muscular structures of different ages, functions, and degrees of vulnerability. Hence we are really back again in 1913 when Semon himself could only conclude that the earliest destruction of the abductors in progressive lesions implies that there exists an actual difference in the biological composition of the laryngeal muscles.

Perhaps a study of phonetics might throw some light upon the problem. The appearance of the so-called "glottal stop" is an early but important landmark in the development of infant speech and is mediated by structures which exclude food from the air passages. Their ancillary influence upon phonation is to evoke the guttural sound [k] (unvoiced) and more especially the voiced guttural sound [g]. The vocalization of newly born babies is chiefly made up of vowel sounds. Consonantal sounds appear later. Although more data are required, it is possible—if not probable—that the voiced and unvoiced gutturals are among the earliest of the consonantal cries and appear within the first month. We believe that in early infancy, vocalization denotes discomfort, and silence means satisfaction. But at a little later date the infant becomes capable of emitting comfort noises. These are symbolized by consonantal sounds of later appearance. In other words the earliest consonantal sounds are mediated by the glottal stop, i.e. the adductor elements, and connote discomfort. The wide range of abductor sounds associated with comfort appear later.

adductor fibres, or even exclusively, in cases of undoubted central or peripheral injury or disease of the roots or trunks of the pneumogastric, spinal accessory, or recurrent nerves".

But unfortunately he had been forestalled a few months before by Rosenbach, who upon the basis of a solitary case of carcinoma of the œsophagus had stated "... in compression of the trunk of the recurrent, the function of the abductors suffers first, and that of the adductors is implicated only later on".

The eponymous term Semon's Law has rightly passed into medical terminology, though some Continental sticklers may continue to speak of the Rosenbach-Semon law, or even the Gerhardt-Rosenbach-Semon law.

With the passage of sixty years it is not surprising that cases should occasionally be reported which show themselves (or appear to) as exceptions to this law. Perhaps it is a matter for wonder that the exceptions have been so few. But for this reason some—like the Chevalier Jacksons—would prefer to speak of Semon's rule rather than Semon's law, a distinction which might be regarded as a quibble.

Perhaps the majority of those exceptions comprise pseudobulbar laryngeal palsies, due to supranuclear lesions. This at least is what Semon afterwards affirmed, namely in 1913, when he emphasized that his law only concerned the laryngeal nerves from the nucleus downwards. Semon must, however, bear some of the blame for this misconception, for all his early papers on the subject referred to both peripheral and central lesions. By "central" Semon probably meant "nuclear" lesions, though most present-day neurologists might well assume these to refer to supranuclear locations.

Anyway the point is a good one, and the fact remains, I think, that supranuclear affections of the nucleus ambiguous do not necessarily behave according to Semon's law, e.g. in cases of pseudobulbar and progressive spastic bulbar paralysis, as shown by Collier, Critchley and Kubik, and others.

Later authors have read more into the law than Semon originally stated in that it is now taught that with progressive affections of the recurrent laryngeal nerve, the abductors are the first to be affected, while the tensors of the cords are implicated later, and the adductors last of all. Or, in terms of the muscles involved, the crico-arytenoideus posticus suffers first, then the thyro-arytenoideus, and lastly the crico-arytenoideus lateralis. The arytenoideus, having a bilateral nerve supply, is not affected in unilateral cases, while in bilateral disease it is affected very late.

Experimental physiologists have since shown that the law holds true for processes other than pressure effects or disease. Thus the abductor components of the recurrent laryngeal nerve have proved to be more sensitive than the adductor elements to such influences as drying (Risien Russell) and to freezing (Gad and Fränkel).

The many and diverse views that have at various times been proposed to explain Semon's law may best be arranged in chronological order.

Muscular hypotheses.—(a) Abductor group requires a greater volume of blood (Clausberg). (b) Abductors differ in chronaxy from the adductors (Tarneaud). (c) Abductors early lose their excitability after death (Jeanselme and Lermoyez). (d) Adductors are mechanically better placed than the abductors (Gowers). (e) Abductors suffer because the nutrient artery is involved (Robinson).

Location of abductor fibres within the recurrens.—A more peripheral siting of the abductor fibres suggested (M. Mackenzie).

Double innervation of abductor group.—(a) From spinal components (Tissier). (b) From superior laryngeal nerve (Cohen Tervaert).

Abductor paresis is really an irritative adductor spasm or adductor contracture (Krause). *Glottis-closure is subserved by a powerful cortical centre* (Bosworth; Risien Russell; Horsley).

Abductor proclivity is an instance of a general axiom that extensors are more vulnerable than flexors (Ferrier).

Glottis-closure is phylogenetically an older function of the larynx than is the opening of the glottis (Negus).

Some of the foregoing suggestions can be disposed of quickly.

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in a state of very restricted activity, but he had not seen her for a long time. The other one was the case to which Mr. Davis referred. He thought for a time the phrenic-recurrent union had succeeded, but he had lost sight of her, and it was evidently a failure. Therefore only 1 of the 5 cases from a surgical point of view was successful. Unless the paralysis was of very short duration it was unlikely that a surgical success would be attained.

When he reported these results in 1939 he suggested that from a practical surgical point of view they might get all they wanted in relieving the patient's respiratory obstruction by fixing one of the cords in an abducted position. The operation he then suggested was to expose the arytenoid cartilage, abduct the vocal process, and fix it in the abducted position. In order to do that an incision was made down to the pyriform fossa by retracting the ribbon muscles forward and incising the inferior constrictor along the posterior edge of the thyroid ala. It was possible thus to expose quite easily from the outside, without opening the pharynx, the crico-arytenoid joint, which was opened and the arytenoid was exposed. The posterior edge of the ala should be excised.

The difficult part was to drill a hole in the arytenoid cartilage in which a suture was put near the vocal process to draw the vocal process out. The arytenoid cartilage was fixed in abduction by drilling two holes in the thyroid ala through which the ends were passed and tied outside the ala. Mr. Archer gave him the opportunity of doing that by sending to him from Manchester in 1942 a woman aged 40 who had compensated mitral stenosis and had had a thyroid operation, and eighteen months later a tracheotomy on account of double abductor paralysis causing stridor and distress. He carried out the operation described, and within a few days the tracheotomy tube was withdrawn and she breathed comfortably. She had written later stating that she was quite comfortable and had a good voice.

It was important that nothing should be done to disturb the intact laryngeal mucosa, and that was why all the operations devised for excising the cord were failures; one simply replaced the paralysed cord by a fixed scar. He had one patient, a woman from the North of England, who had a palsy with a tracheotomy, and she proved to be a person with acromegaly. In carrying out the operation the arytenoid cartilage became dislocated and he removed it altogether and fixed the cord, as he hoped, in an abducted position. In that case the relief was short-lived; she did get rid of the tracheotomy tube, but it had soon to be replaced. But on the basis of the first case the first method seemed to him quite a practicable one.

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Gavin Livingstone recommended the clinical use of the electromyograph as an aid to diagnosis. A long bipolar needle was inserted through a laryngoscope under local anæsthesia into the adductor and abductor group of muscles and the nerve impulses reaching the muscles were recorded.

In one case of apparently complete paralysis of the cord, the myograph showed normal nerve impulses coming through, but no movement was seen—the condition not being due to a nerve lesion.

There was no real technical difficulty in the needling, but the electrical recording and cathode ray amplification needed expert supervision.

T. B. Layton said that he liked the term "idiopathic" better than "paralysis of unknown origin". He wondered whether there were such things as idiopathic paralyses of the larynx and would suggest that all these cases called idiopathic were really cases of fixed joints. An arthritis of the joint caused the cord to be fixed during the acute stage, from which it recovered. He had seen one such case in a young doctor who had been told by another medical man that he had an idiopathic paralysis of the cord. This patient had been spending a winter holiday in Switzerland, and after playing in hot sunshine he was seized with a chill as the sun went down behind the mountains and he felt a severe pain in his neck and a sensation of frightful coldness. From that moment he became hoarse. The speaker suggested to him that what was wrong was a fixed joint, not a paralysis of the cord, and that it might come right, and so it proved. A case of undoubted paralysis of the cord was certainly a serious, and probably a grave, lesion.

Lionel Colledge, in reply to a question as to what sort of voice these people had after operation, said that in the woman whose case he had described the voice was a little rough but strong. Generally the patients with palsies had normal voices after a certain time for adaptation. They adapted themselves to talking with one cord, and the voice, perhaps with a little speech therapy, became normal.

J. Angell James described the case of a soldier who had been wounded by a mortar bomb, a fragment of which had entered his neck through the right posterior triangle.

Much more work is required along these lines but already it seems as though phonetics might produce a confirmatory piece of evidence and serve to bring Semon and Negus still further into line.

E. D. D. Davis: The term "idiopathic" means without pathology and without cause. Paralysis of the laryngeal nerve of unknown or obscure origin is what is really meant. Paralysis of the left or right recurrent laryngeal nerve is common in pulmonary tuberculosis, caused by enlargement of the mediastinal glands. The tuberculous lesion may heal and the paralysis may disappear or remain. Similarly cases of syphilis causing double abductor paralysis recover with treatment and in both diseases the original cause of the paralysis may be obscure. Paralysis of the laryngeal nerve occurs in thrombosis of the posterior inferior cerebellar artery and this paralysis sometimes remains after all the other symptoms have disappeared. Bilateral or unilateral abductor paralysis arising from enlarged mediastinal glands has occurred on very rare occasions in children. Such cases of laryngeal obstruction have been admitted to the Fever Hospital for suspected diphtheria and a tracheotomy has been necessary. Mr. Ridout showed a post-mortem specimen of such a case at this Section many years ago. Enlarged mediastinal glands had stretched the nerves.

The enlarged glands are not always easily recognized by X-ray photographs and these cases may be described as of obscure origin. I have seen 5 cases of double abductor paralysis following thyroidectomy which I have kept under observation for some years.

The first case developed double abductor paralysis a short time after the operation. This woman had a tracheotomy performed and was more or less an invalid all her life and did not attempt to go to any social function. The next case, a young woman of 22, kept her household awake at night with her noisy stridor. She was embarrassed on exertion and had attacks of dyspnoea. She married and when she was pregnant it became necessary to terminate the pregnancy owing to the difficulty in breathing. The right phrenic nerve was united to the right recurrent laryngeal nerve and when seen a few years later there was no movement of the right cord. The patient thought she was better but there was no alteration in the abductor paralysis. This patient has attacks of bronchitis of the base of the right lung with retention of secretion. These cases after some years show relaxation of the adductor muscles and particularly the interarytenoides or transverse muscle. The larynx shows an elliptical chink between the anterior two-thirds of the vocal cords, and a larger triangular area between the arytenoids, making almost normal respiration possible. The question is, can the patient wait for this happy result without a catastrophe?

If tracheotomy is performed it should be a low one and a tracheotomy tube would have to be worn for many years.

Double abductor paralysis of syringobulbia is not always complete and occasionally there is slight movement of one or both cords and also the adduction of the cords is not so marked.

Lionel Colledge said that he had been interested for a long time in the question whether it was possible to restore movement to a paralysed cord. It was not of much consequence where the paralysis was unilateral, because that only very exceptionally produced any respiratory difficulty. Attempts were made by Ballance and himself in 1925 to discover whether by any form of nerve anastomosis movement could be restored to one or other side. Most of the nerves of the neck were tried, including the descendens noni which had been mentioned. No good result was obtained with the descendens, but satisfactory results were claimed in America. When the recurrent was divided either the cord might remain in its previous position, median or paramedian, or it might be moved out, depending on the length of time of the paralysis and the degree of contracture of the muscles. If the contracture was firmly fixed at any one position the cord would not move out. That was all that happened with the descendens.

They tried on monkeys the effect of using the phrenic, which seemed more promising, because respiratory impulses were going down the phrenic, and therefore there was more hope of restoring respiratory movement to the cord. Experimentally it worked very well in animals. In one case it was possible to show a monkey with both cords moving quite freely on the phrenics. Therefore he tried operation on the human being on this experimental basis. He had carried it out on 5 patients. In 2 nothing happened at all. One was a woman with a bilateral recurrent paralysis following thyroid operation, and there was no result. In another there was the same thing, and in both these cases a tracheotomy was done. The third case was a man with what Mr. Davis would call paralysis of unknown origin. The cord moved out (in the other 2 it did not move at all), but he got an infection of the arm about six weeks later to which he succumbed.

The other 2 cases were both in young women. One, he felt sure, succeeded quite well because the patient was able to dance and lead quite an active life after being

JOINT DISCUSSION No. 1

Section of Orthopædics with Section of Surgery

Chairman—W. B. FOLEY, F.R.C.S.

(President of the Section of Orthopædics)

[February 5, 1946]

TREATMENT OF ACUTE OSTEOMYELITIS WITH PENICILLIN

R. Vaughan Hudson: Since March 1943 we have submitted to laboratory and clinical investigation 400 cases of penicillin-sensitive infections at various sites in the body. 37 of these cases happened, or proved to be, acute or subacute osteomyelitis.

In 30 cases the organism causing the infection was the *Staphylococcus aureus* and in 7 *Streptococcus pyogenes*. In the majority the infection had been present for some days, in only two was the disease seen as early as the fourth day, and in one case it was a hundred and fifty days before we received the patient. The youngest patient was 1 year old and the oldest 70 years of age.

It must be agreed that osteomyelitis is one of the most tragic of diseases which can affect the children of any nation, and it is also surprising the number of adults who are primary sufferers from this disease.

There are certain points about the causation of osteomyelitis which are perhaps not well known. First the history given by the patients or their relatives is often misleading; with deliberate questioning it is found that the initial cause of the illness, a carbuncle, boil, or respiratory infection, has been forgotten and healed three to four weeks before the identical organism produced the train of symptoms known as acute osteomyelitis.

Second a persistent septicæmia of an apparently unknown origin is more likely than not to be due to an osteomyelitis, and, alternatively, if a septicæmia is permitted to persist it will more probably than not give rise to an osteomyelitis. In 6 of our cases, had penicillin not saved the life of the patient and given time and opportunity for the feeding focus to be discovered in one of the bones, the patient would have died with the cause of his malady unrecognized, for it is not usual for every bone in the body to be examined in the post-mortem room by the pathologist.

We have not received for treatment cases of established acute traumatic osteomyelitis such as have been seen by many who have worked in the Field. Accidental trauma, however, has undoubtedly focalized the site of infection to a bone in patients who were carriers of an active organism. Surgical trauma by the dissemination of infection, for example the surgery of infected accessory air sinuses, soft tissue infections, and even such a trivial operation as the removal of a nail for paronychia, has been the immediate or delayed cause of 20% of all our cases.

The right vocal cord was completely paralysed, and a skiagram showed a fragment measuring 4 mm. by 2 mm. in the neighbourhood of the right transverse process of the sixth cervical vertebra. He had considerable discomfort in the neck and surgical intervention was thought justifiable. The carotid sheath was exposed and the fragment found embedded in the medial half of the vagus nerve. The fragment was removed and the sheath repaired, and it was hoped that there might be regeneration of the nerve and recovery of the vocal cord. A year later he wrote that his voice had completely recovered, but only two days ago the man came to be seen, and the cord was still paralysed.

The President said the discussion had proved extremely interesting. Cases of bilateral laryngeal paresis were, fortunately, very uncommon. Unilateral paresis rarely gave trouble apart from loss of voice for a short period. The voice cleared when the other cord compensated but the paresis usually remained complete. He had in mind two ministers, both of whom have unilateral vocal cord paresis, and yet they have apparently normal voices. They were both voiceless for a short period only. In one case of sudden onset of bilateral paresis an urgent tracheotomy had to be performed and the patient (who was a jeweller) made his own tracheotomy tube with a small valve across the mouth controlled by a fine "bowden" wire so that he could speak normally without closing the tube with the finger.

Following on the publication of Dr. Irwin Moore's paper in 1923 (*Jnl. Laryn. & Oto.*, 38, 236) he (the President) had tried the anterior operation. One case was almost successful but he split the cartilage in the middle line and by some mischance one cord was replaced rather below the other. The result was quite good except that the voice was what might be called a forced whisper only.

He had tried grafting the anterior end of the cords but without success although one case gave quite good results for about a year. He had only tried the posterior route once and although the result seemed quite good the patient had a lot of stridor and thought he was better with the tracheotomy tube.

The President agreed with Mr. Layton that some of these so-called idiopathic pareses were really joint infections.

Maxwell Ellis, in reply, agreed that "idiopathic" was not a satisfactory term, but at least they knew what it meant. It was very interesting that Mr. Colledge in 1939 should have embarked on the precise procedure that King described in the same year with a report of 24 cases. King did not bore a hole through the vocal process, because that was a difficult procedure technically. It caused fracture and was not easy to carry out. He ran the suture round the inner side of the vocal process and then did precisely what Mr. Colledge had described. The point was not to enter the larynx; if one did scar tissue formed. The second case which Mr. Colledge described followed the technique which Kelly employed in America.

Some speakers had suggested that recovery was an instance of functional, not anatomical, cure. Undoubtedly a number of these unilateral cases did resolve and the cord returned to normal.

If Mr. Layton had put his question before Mr. Livingstone had spoken he would not have known how to answer it, but Mr. Livingstone had described an electro-myographic method of detecting the response of a nerve, and that might distinguish between cord paralysis and joint fixation. Without being too scientific and dogmatic he felt sure Mr. Layton would agree that on the basis of clinical experience, while there were a number of things not very easy to describe or define, one might be quite sure that one was dealing with a particular condition, generally on the basis of repeated examinations at different times.

The whole point of the Kelly operation of removing the arytenoid was to give a good airway posteriorly and to preserve a fairly good voice.

The President seemed to have gone the rounds of these various operations and he would have liked to have heard him speak on them at greater length.

Macdonald Critchley, also in reply, said that he would like to make a plea for a most meticulous examination of the nervous system in all obscure cases of laryngeal palsy, because such might be the first sign of a tabes or of several other neurological conditions. As a neurologist one was often asked to see cases of paralysis of the larynx combined with lesions of other cranial nerves. Such cases were probably due to a virus infection. There was no reason why there should not be a virus affection of one single cranial nerve, e.g. the vagus, or recurrent laryngeal. Bell's palsy was probably an example of such. He had no doubt that members were also familiar with cases of recurrent laryngeal palsy in returning prisoners of war from Japan. Many showed signs of nutritional deficiency with bilateral blindness, deafness, dysæsthesia of the extremities, and recurrent laryngeal palsy.

the time of the surgery upon the phalanx itself, although obtaining primary union developed ankylosis of the joint, but the tendons which were bathed in pus recovered their function.

When we come to the systemic dosage of penicillin used I would again state that one is doubtful of the permanency of the cure in the majority of these cases. The average dose was 20,000 units of penicillin administered intramuscularly every three hours day and night for an average of ten to twelve days. Later in the series this dose of 20,000 units was raised to 60,000 units three-hourly, and the results were definitely better.

When we come to the duration of treatment and consider the amount of work that penicillin has to do to reach the organisms within the infected avascular tissue, it is probable that the duration of treatment is nearer to that of subacute bacterial *endocarditis* in which we did not get permanent results until a minimum of twenty-one days was reached.

Local penicillin as an adjunct to systemic penicillin made no difference to the results. In fact the recurrence rate when penicillin was used in addition to systemic penicillin was statistically higher than those who had systemic penicillin only.

Systemic penicillin, therefore, as far as we know, localized infection to the initial site in the bone, and complications were either cured or prevented. This has also been true of prophylactic systemic penicillin as far as our 11 cases can assist us in this opinion.

Primary union has been achieved in the face of infection and the dissemination of infected material prevented. In prophylaxis the uniformly satisfactory results obtained in soft tissue lesions liable to cause an osteomyelitis, and the use of a systemic penicillin "umbrella" in the surgery of infected lesions, should help to lessen the incidence of this disease.

Early diagnosis and early treatment with penicillin will prevent infection of avascular tissue and assist in the absorption and remodelling of infected avascular tissue.

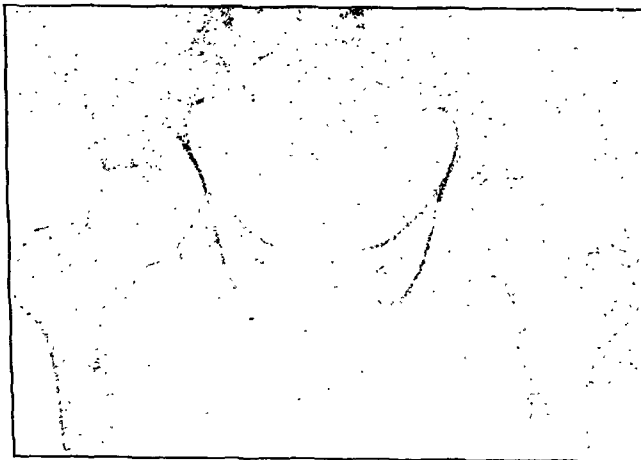
At certain sites in the body owing to the proximity of vulnerable tracts or cavities and in the later stages of the disease, radical extirpation of infected tissue if appropriate and accessible will, under the cover of penicillin, still be necessary. Long incisions and drainage without the removal of infected bone appear from our results to be unwarranted.

It is my conclusion that the future holds great promise for the employment of penicillin in all forms of penicillin-sensitive infections, and this includes infections that happen to alight in bone.

Once more I must pay the greatest tribute to Sir Alexander Fleming and Sir Howard Florey and his co-workers.

I am indebted to the Medical Research Council for penicillin used in this research.

CASE I (X-ray a).—D. G., aged 14. Admitted December 1943 on fourth day of illness. Septic finger two weeks previously. Blood culture *Staph. aureus*, effusion left hip-joint sterile. Pyrexia, severe pain and inflammation upper third of femur. Systemic penicillin. No immobilization. Rapid recovery. X-ray six months after onset. Two years since onset; full function; no recurrence.



CASE I (X-ray a).

It is fit and proper that the results of penicillin therapy should be regarded with the greatest reserve. The vagaries of this disease are only too well known. This is exemplified by one of our own cases who after many vicissitudes and surgical operations, recovered from a gunshot osteomyelitis of the femur in 1918 and remained well for twenty-five years before he spontaneously developed a recurrence of his disease in the fourth year of the Second World War. All of us have known cases to recur at frequent intervals either in the same bone or at unsuspected sites in other bones during the course of the patient's lifetime. It is also our experience that the severity of the disease varies very much from year to year and from patient to patient. In one there may be multiplicity of foci, in another the whole of one bone is affected, and yet another the lesion is localized to a small area in one bone only.

The organism has a peculiar property of hibernation with irregular periods of exacerbation. If the diseased bone is operated upon during the period of hibernation the pathologist is unable to culture the organism, if, however, the patient is operated upon during the period of exacerbation the organism is cultivated with certainty. In both the acute and in the chronic disease the importance of the soft tissue element is apt to be forgotten for there is an extensive change in the soft tissue within the cancellous lattice-work, in the medulla, the periosteum, and commonly in the circum-osseous soft tissue surround.

It is this predominant change in the soft tissue which renders the diagnostic value of X-rays negligible or imperfect, and is the reason that there is a "lag period" in the visible change in the cancellous and compact tissue portraying an event of the past without relation to the present condition of the patient.

For the purposes of discussion I have subdivided these 37 cases into three groups: acute hæmatogenous osteomyelitis, acute recurrent osteomyelitis in which the patient had previously suffered from an osteomyelitis, and subacute recurrent osteomyelitis.

In the latter two groups it is obvious that a gross change has occurred in the soft tissue and in the bone prior to the acute or subacute exacerbation of the disease. This gross change is paralleled by patients submitted to treatment in the late stages of their first attack of hæmatogenous osteomyelitis. It is only in the early stages of acute osteomyelitis that penicillin has its greatest opportunity of assisting the patient.

Our method of treatment, however, in all cases was to institute penicillin and wait and observe the progress of the case. It soon became apparent that penicillin swept the organism from the blood-stream and reduced the acute lesion to that of a chronic lesion. The subsequent fate of the patient depended upon the management of this now chronic osteomyelitis.

This was true of 34 of our 37 cases. The exceptions were 3, a boy of 12 months and a man of 37 both of whom already had bilateral metastatic lesions in the lung and other complications, who died, and a man of 34 suffering from acute osteomyelitis of the os innominatum and head of femur, a failure owing to under-dosage.

Of the 34 remaining cases, in 13 penicillin alone proved successful and so far without recurrence of the disease. In a further 7 as a process of resolution, an abscess formed in the soft tissue and was treated by stab drainage. 2 of these had a subacute exacerbation three months after their discharge from hospital but responded to a second course of penicillin. These 7 cases remain free of recurrence. A total of 20 out of 34 cases.

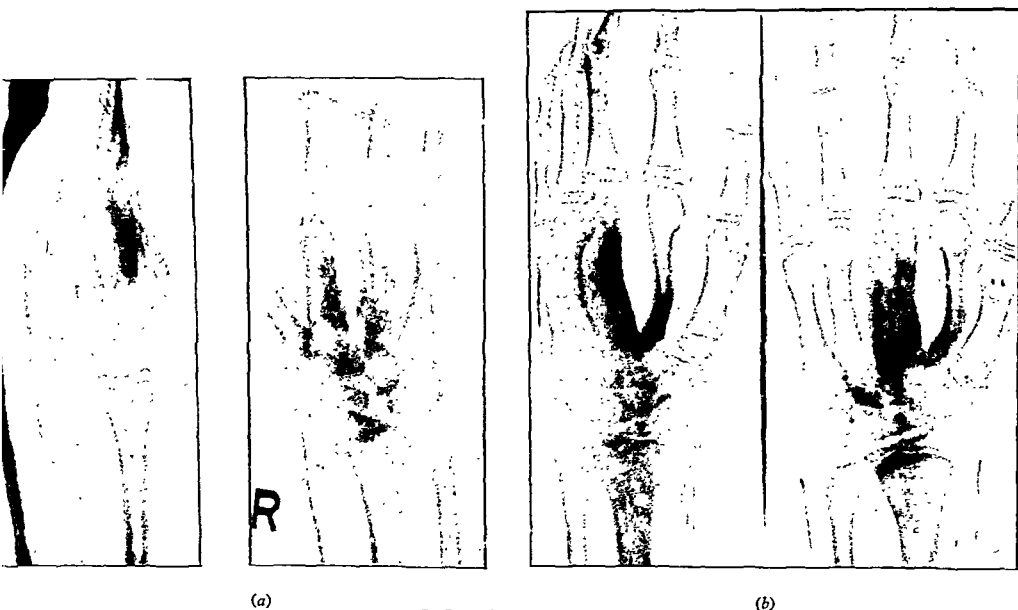
In 7 further cases the indications were such that under cover of the original course of penicillin the dead and infected bone should be removed. These indications were the proximity of the brain, pleura, or tendon sheaths. All visible dead and infected tissue was removed with primary suture and temporary drainage, and primary union achieved. 1 of these cases had a doubtful subacute recurrence three months later which responded to a second course of penicillin. All 7 remain well.

In 1 other case penicillin and drainage having reduced the acute lesion to the chronic state, and as a deliberate policy, the patient was discharged to be readmitted three months later for extirpation of the now well-demarcated dead bone and primary suture. He also obtained primary union and is free from recurrence.

In the 6 remaining cases an attempt was made to see whether the drainage of bone and soft tissue as a primary procedure under the cover of penicillin would be an improvement upon penicillin only or penicillin and stab drainage. This proved highly unsatisfactory in that generous incisions or multiple drainage which failed to remove all infected bone gave us our worst results. 5 of these 6 cases have a persistent chronic sinus and require radical surgery.

The complications already present in these cases are too varied and numerous to particularize, empyema, jaundice, peri-arthritis infection in many but intra-arthritis infections in only 4 cases of proved certainty. 2 recovered full function of their knee-joint without surgery, and 2 in whom the interphalangeal joints had to be opened at

CASE IV (X-rays a and b).—M. S., aged 10. Admitted November 1943 on forty-third day of illness with request for amputation. Pyrexia and acute spreading inflammation; hand like a boxing glove and forearm grossly swollen, sinuses in palm. Culture *Staph. aureus*. X-ray (a) Systemic penicillin, loose bone and sloughs removed plus local penicillin daily via catheter. Rapid recovery, discharged with one chronic sinus. For deliberate readmission when general condition had improved and lesion well demarcated. Six months later systemic penicillin hemi-diaphysectomy and removal of infected bone, primary suture. Primary union. X-ray (b) one year after onset. Two years and three months no recurrence, soft mobile hand and joints but power equivalent to 30% of normal only.



(a)

CASE IV.—X-rays.

(b)

TABLE I.—LESIONS OF BONE—48 CASES.

(March 1943—June 1945. Average Follow-up One Year and Three Months.)

THE RESULTS WITH PENICILLIN ADMINISTERED BY THE SYSTEMIC ROUTE AS A PROPHYLACTIC IN 11 CASES OF COMPLICATED COMPOUND FRACTURES AND IN THE TREATMENT OF 37 CASES OF ESTABLISHED INFECTION IN ACUTE PRIMARY AND RECURRENT ACUTE AND SUBACUTE OSTEOMYELITIS.

			Did not recur	Fate of remaining 12 of 48 cases	Follow-up Healed and no recurrence	Chronic sinus
A = Penicillin — no surgery	=	A	13 of 15	1 died * 1 failed†	13	
C = Penicillin + stab drainage of the soft tissue abscess	=	C	5 of 7	2 recurred in 3/12 and responded to 2nd course A	7	
B = Penicillin + radical extirpation of all the visible dead and infected bone. Primary suture and temporary drainage	=	B	6 of 7	1 recurred in 3/12 and responded to 2nd course A	7	
B ¹ = Prophylactic penicillin + adequate and deliberate surgery in compound complicated fractures. Primary suture	=	B ¹	11 of 11		11	
D+E = Penicillin + drainage of bone and soft tissue without the removal of dead and infected bone. Primary suture temporary drainage	=	D+E	1 of 8	1 died * 1 treated by A + B primary union. 5 failed 2nd course A and require A + B	2	5
			36 of 48		40	5

SUMMARY OF RESULTS IN 48 CASES.

Treatment	Healed and free of recurrence	Failed or chronic sinus
A+C+B+B ¹	38	2 (1 death)
D+E	2	6 (1 death)

* Deaths 1A aged 1. Shaft of tibia, bilateral bronchopneumonia and mediastinitis.

† Failure 1A aged 37. Frontal sinusitis, vault of skull-subdural abscess, bilateral bronchopneumonia.

† Failure 1A aged 35. Os innominatum and head of femur. Underdosage.

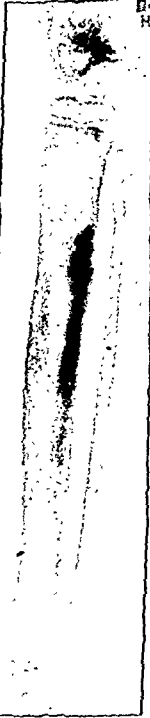
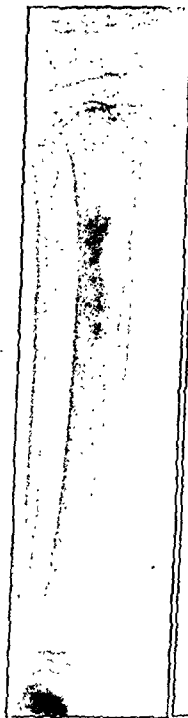
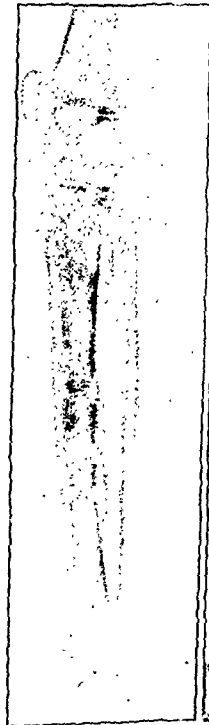
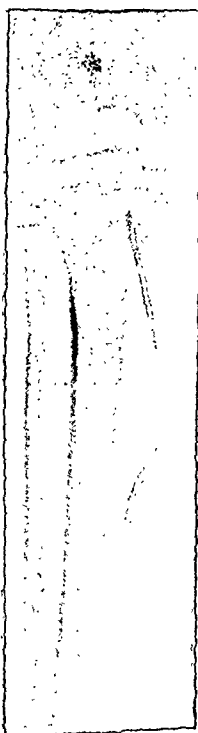
CASE II (X-rays a and b).—E. C., aged 37. Admitted May 1945 five weeks after onset of a septic abortion. Blood culture *Staph. aureus* had previously had $2\frac{1}{2}$ million units of penicillin. On admission subacute osteomyelitis of right upper third of femur. X-ray (a) Systemic penicillin refused immobilization (b) X-ray five months later. It is ten months since onset, full function and no recurrence.



CASE II (X-ray a).

CASE II (X-ray b).

CASE III (X-rays a, b and c).—D. S., aged 7. Accidental trauma. Admitted October 1943 on tenth day of illness with coma, meningismus, swollen inflamed lower right leg. Blood culture *Staph. aureus*. X-ray negative. Systemic penicillin, no immobilization. Five days later stab drainage of "cold" soft tissue abscess, local penicillin—as an adjunct—via catheter daily. X-ray (a) fifteen days later. Twenty-first day up in chair. X-ray (b) fifty-five days after onset. Fifteen and a half weeks after onset subacute recurrence. Aspiration=*Staph. aureus*. Second course of penicillin rapid recovery. (c) X-ray two years after onset. Now two years and five months since treated; remains well; full function.



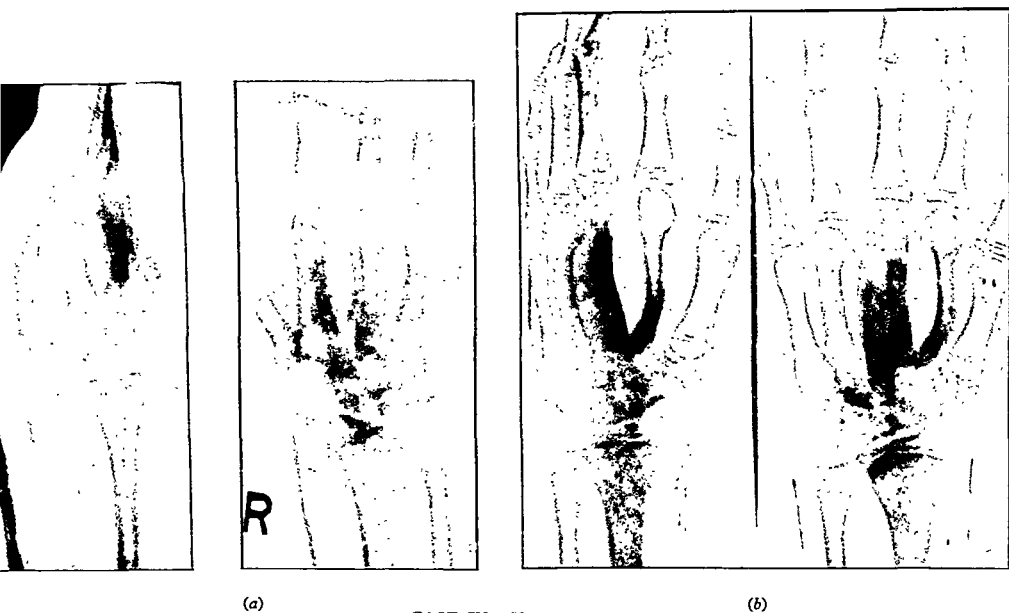
(a)

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FOLLOW-UP

TABLE II.—THE TREATMENT OF OSTEOMYELITIS.
HEALED AND FREE OF RECURRENCE

		Healed and did not recur										
		B										
		A										
		Penicillin only										
		Penicillin + extirpation all infected bone suture and drain.										
		C										
		Penicillin and drain, bone and soft tissue										
		D+E										
		Deliberate readmission expiration bone										
		Subacute recurrence Resp. 2nd course penicillin only										
		Efficient full work or full school										
		Remain healed and free of recurrence										
		Efficiency limited by infection										
		Chronic sinus										
		Efficiency limited by infection										
		1 D+E										
		1 D+E										
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Dr. J. Trueta reported the results of a series of 30 cases of acute osteomyelitis treated with penicillin over a period of eighteen months at the Wingfield Morris Orthopædic Hospital. The cases were not selected, the duration of the disease before admission varied from thirty-six hours to eight weeks; all of the cases were children except 3 who were over 21. At the beginning of the series the effect of penicillin treatment alone was tried. Adequate immobilization was used, but surgery was withheld. In cases where there was no abscess at the focus, when treatment was begun, penicillin alone cured the disease, provided that the dosage was adequate and the duration of the treatment long enough (1 case in which treatment was stopped after four days when all symptoms and signs had disappeared relapsed but was cured by a second and longer course). In cases where there was already an abscess present at the focus when treatment was begun, the general recovery was slower and even after apparent clinical recovery from the infection the disease could be seen radiographically to spread sometimes for eight to ten weeks before repair began. Pus aspirated from the focus a month after onset showed that staphylococci were still present in large numbers.

The penicillin was therefore supplemented by surgery in the later cases admitted with abscesses and the results were very satisfactory. It was found that if as much pus as possible was evacuated at operation from without the bone and from within by drill holes, no new pus was formed and primary suture was safe. The cases treated in this way recovered from the general infection very much more quickly than those cases with retained pus, and the spread of the disease in the bone no longer occurred, repair began sooner and was more rapid as there was less area of bone involved.

The penicillin in the series was given usually by intramuscular drip. At first 100,000 units in twenty-four hours was used as standard dosage, but with increasing supplies the initial dose was increased to a maximum of 400,000 units in twenty-four hours. It was hoped that with this dosage the bactericidal action of penicillin would be used and the impression was that the initial illness was terminated more abruptly with the high dosage both in the drained and undrained cases. The total dose was not affected by the heavy initial dose as it was found that in these cases the course could usually be terminated earlier. The average dose was 1,000,000 units though it varied from 600,000 units to 3,000,000 units. The shortest effective course was six days, and the longest course was fourteen days.

A standard routine was adopted. Cases admitted without abscess formation were treated by penicillin alone; cases with abscess at the focus were treated with penicillin and with surgery, which included drilling of the bone and primary suture after evacuation of as much pus as possible. Immobilization of the affected part was always used.

The results were encouraging. There was no death in the series. No case developed a metastatic focus, or a local joint invasion after admission. 7 of the cases were suitable for penicillin treatment without surgery, the remaining 23 required surgery. Of these, 2, early in the series, were treated by aspiration alone, and had extensive bone damage. One was readmitted ten months after onset with an abscess connected with the involucrum. Of the 21 wounds, 18 healed without sinus formation, 1 (unsutured) became secondarily infected and required drainage after healing, 2 with extensive bone damage on admission developed sinuses. 4 sinuses persisted, 2 from undrained and 2 from drained cases. There was normal function in 28 of the 30 cases. The exceptions were: an osteomyelitis of femur admitted with septic arthritis of the knee in which the knee range was 5 to 90 degrees; and an osteomyelitis of the humerus of fulminating type admitted thirty-six hours after onset, with involvement of the whole shaft of the humerus; there was full range of movement at the joints but she was still in hospital thirteen months after onset with a persistent sinus.

The results of the treatment of acute osteomyelitis with penicillin were so good that it was fair to say that the disease had been altered and that we now needed a new standard for our results. It was no longer right to congratulate ourselves on a low rate of mortality, metastases, joint involvement and sinuses. There should be no such rate. Improvements would be obtained if patients could be admitted earlier, and now that it was known that there was a cure for the disease if it were treated early, doctors would admit cases for treatment earlier than they had done hitherto; one should no longer wait for the appearance of an abscess. Early cases could be treated by penicillin alone; and might leave hospital, perfectly normal, after three weeks. For later cases, however, surgery was still important, and it should include bone drilling and primary suture.

Dr. Trueta had been impressed by the figure for joint involvement of 25% in a penicillin series where aspiration of abscesses and the metaphyses had been used instead of incision

and drilling, and was himself convinced that so long as cases were admitted with abscesses present, the evacuation of the pus from within and without the bone was an important part of the treatment, in preventing both local joint involvement and spread of the disease through the bone. He stressed the importance of the periosteal blood supply in the repair of the bone, and pointed out that unless the subperiosteal pus was adequately drained, the periosteum was held away from the bone, and could play no part in the repair except to form an involucrum walling off the diseased bone from the external blood supply, and leaving it dependent on the nutrient artery which was probably, at least in part, thrombosed.

Mr. E. C. B. Butler: The treatment of acute osteomyelitis with penicillin may be considered under three headings, the bacteraemia, the toxæmia and the bony lesion.

The bacteraemia.—In 1940 I reviewed the immediate and late results of 500 cases of acute hæmatogenous osteomyelitis admitted to the London Hospital between the years 1918 and 1937. 127 died, a mortality of 25%. In 92 cases a post-mortem was performed, 89 deaths were due to staphylococcal pyæmia, two died during operation and one had bronchopneumonia.

Investigating cases of staphylococcal bacteraemia, many of which were osteomyelitis, Dr. Valentine and I (1943) found that repeated quantitative blood cultures were of considerable value in assessing the immediate prognosis in patients suffering from a persistent blood-stream infection.

In a series of 30 cases we were able to differentiate three groups on a basis mainly supplied by quantitative cultures.

Group 1 consisted of 9 cases of fulminating infection; death occurred in four to five days, colony counts in the blood showed either very high figures 500-1,000 on admission or a rapid rise if the examination was repeated. All died.

In Group 2 the colony count was above 30. The infection was less overwhelming but still serious since only 3 out of 8 cases survived. The deaths took place after three to six weeks from the formation of secondary foci in vital organs particularly the lungs.

Group 3 was characterized by a low colony count of less than 20, the blood usually soon became sterile, there were only 3 deaths in 13 cases, showing that recovery was the rule.

Another point of interest was the presence of a persistent primary focus of infection in cases of acute osteomyelitis associated with bacteraemia. In 1939 we suggested that these foci rather than the infected bone may sometimes be held responsible for the maintenance of the bacteraemia. In severe cases it was our custom to excise or drain these foci in the hope of cutting off the source of the blood infection. In a few cases this treatment appeared to be effective.

The effect of the introduction of the sulphonamides, particularly sulphathiazole appeared to lessen the immediate mortality in our cases. In 15 consecutive cases of osteomyelitis treated with sulphathiazole there was 1 death but only 5 patients had proved staphylococcal bacteraemia which in 1 successful case rose to 97 colonies per c.c. of blood; the patient who died had a colony count of 100 colonies and did not respond to chemotherapy.

Since the introduction of penicillin the story is very different. Altemeier *et al.* (1945) record 34 cases, 20 with a positive blood culture, only 1 died, a late case admitted seventeen days after the onset of the disease. McAdam (1945) describes 40 cases with only 1 death. We have treated 14 acute cases, 7 with a positive blood culture. Unfortunately owing to war conditions quantitative blood cultures were not done on all our patients, the highest figure recorded being 60 colonies. All have recovered.

I have no doubt that the introduction of penicillin has reduced the mortality of this disease from 25% to about 3 to 5% by controlling or preventing the blood infection which so often accompanies acute osteomyelitis and which is the usual cause of death in fatal cases.

Deaths still occur, however, if the diagnosis is not made until pyæmic abscesses have developed in vital organs and are too advanced to respond to treatment. In fulminating cases penicillin therapy should be started within two days if the infection is to be controlled.

Directly the diagnosis of osteomyelitis is made or suspected a sample of blood should be taken for a quantitative culture; the latter, as I have pointed out, indicates the severity of the infection before the commencement of treatment and also provides material for comparison with similar cases treated before the introduction of penicillin.

At present we give an average dose of 100,000 units daily for a period of at least two and generally three weeks. We believe that if the drug is stopped too soon there is a danger of a relapse in the general or local infection.

Small babies tolerate three-hourly injections well but in older children intramuscular drips may sometimes be more satisfactory.

The clinical response is generally rapid, the general condition improves, pulse and respiration fall and the patient's appetite improves. The temperature, however, may persist for some time particularly if there is an undrained focus of pus present in the infected bone or elsewhere in the body.

In our experience the clinical improvement following the administration of penicillin is of a rapid and decisive character not seen in those cases treated with one of the sulphonamides.

We no longer consider it necessary to interfere with the primary focus of infection unless there is a local collection of pus.

Toxæmia.—Before the introduction of penicillin we used to give severe cases intravenous or intramuscular staphylococcal antitoxin which had a high antileucocidin content. This has now been discontinued. Patients should be encouraged to drink plenty of fluids such as glucose lemonade but solid food should not be forced until the child's appetite returns; this generally occurs as soon as the blood becomes sterile.

Small repeated blood transfusions are often useful in the second or third week of the disease to combat the secondary anæmia which is often present in late cases.

Bone lesion.—On admission the affected limb should be immobilized in a splint or splint reinforced with plaster; a complete cast is obviously undesirable at this stage since it prevents repeated examination of the affected bone. Systemic penicillin is then started. We have so far observed 3 clinical end-results.

Group 1: Complete resolution. In these patients the temperature and pulse rapidly return to normal, pain and swelling of the limb disappear in a few days. An X-ray taken in the third week shows either nothing abnormal or else slight subperiosteal thickening. At the end of four weeks the child is apparently quite well; prolonged rest in bed and immobilization of the limb are not required. 3 cases of this type have been treated, they have remained quite well for twelve months after their illness. To achieve this gratifying result diagnosis must be made early and treatment commenced within two or three days of the onset of the disease. Similar results following the use of the sulphonamides were almost unknown.

CASE I.—Girl aged 9.

18.10.44: Four days' pain in the upper thigh, for a week previously she had a boil on the end of her nose.

On admission.—Ill but not delirious child with subsiding boil on her nose. Swelling and intense tenderness over upper third of right femur.

Blood culture: 60 colonies of *Staph. aureus* per c.c. of blood.

Treatment.—Legs immobilized in a double abduction splint. 100,000 units of penicillin given every twenty-four hours for a total dosage of 700,000 units.

At the end of this rather short course her pulse was normal, only slight pyrexia remained, still slight tenderness over femur.

25.10.44: Temperature normal.

1.11.44: All signs of local and general infection gone, X-ray; No evidence of any bone infection.

Home in four weeks. Has remained well since.

Comment.—This patient responded very quickly to treatment. It is difficult to prove she ever had a bone infection but in view of the physical signs I think we are justified in claiming this to be complete resolution of an early case of osteomyelitis.

Group 2: Extensive bone infection without abscess formation. In this group considerable spread of the infection appears to take place judging by repeated X-ray examinations. Decalcification of the bone spreads for the first few weeks despite the temperature and pulse falling to about normal. After a few weeks the bone gradually becomes recalcified but the process is often slow and may take many months. This is not necrosis since the bone does not die. Small sequestra may form but these are apparently sterile and so far have not given rise to any trouble. These cases require much more care than those in Group 1. At present we advise prolonged rest until the bone appears to have recalcified.

Failure to observe this rule in one of our cases resulted in a painless pathological dislocation of the hip in the fifth week of the disease as the patient was lying in bed. Fortunately reduction was easy and the boy is now recovering with a mobile joint. Pathological fracture or a recrudescence of local infection may also occur if movement is allowed too soon. This point is stressed since some writers maintain that cases treated with penicillin do not require to be immobilized. We think this is dangerous teaching in the presence of extensive bone infection. Despite the alarming X-ray picture in this group there is no cause for undue concern provided that plenty of time is allowed for the affected bone to recalcify. The future of these children is still unknown, such cases require to be followed up for at least ten years before any assessment can be made of their deformity or recurrence rate.

We saw similar cases in patients treated with sulphathiazole, but the progress of the disease was slower and the clinical improvement only became manifest after many weeks. In addition these patients sooner or later generally went on to abscess formation.

CASE II.—Boy aged 14.

Four days, fell and hurt his leg. Two days' pain in left thigh with fever.

1.4.45: Admitted to hospital, very ill boy, swelling and tenderness over upper end of left femur, all hip movements limited.

Blood culture: Positive for *Staph. aureus*, no quantitative culture done.

3.4.45: Penicillin therapy commenced. 100,000 units every day for a total dosage of 1,500,000 units.

13.4.45: Developed an abscess at one of the injection sites which was drained.

2.5.45: General condition good, X-ray shows diffuse disease of neck and upper third of femur. Hip movements apparently painless.

17.5.45: X-ray shows diffuse infection but more marked than before, with pathological dislocation of neck of femur. This was at once reduced and a hip spica put on.

24.5.45: X-ray shows complete reduction.

Remained in plaster until 7.11.45. General condition excellent and after removal of plaster hip movements were possible. At present he has not been allowed to bear weight on the leg but his function is steadily improving.

Comment.—This case illustrates the importance of maintaining immobilization in this type until the danger of dislocation or fracture is over.

CASE III.—Boy aged 14.

Two weeks' boils on neck. Three days' pain in the left hip.

On admission (19.2.45).—Ill boy with temperature 104° and pulse 130. Left thigh swollen and tenderness over upper femur and pelvis. Hip movements impossible from pain.

Blood culture: Positive to *Staph. aureus* but no quantitative culture done.

Treatment.—Leg immobilized in abduction splint with traction. Penicillin 100,000 units daily for a total dosage of 1,000,000 units. During this course his condition improved but his temperature did not settle.

X-ray showed normal femur but area of infection in acetabulum.

14.3.45: Temperature normal, felt quite well. Hip spica applied.

9.5.45: X-ray showed that head of femur was impinging into the acetabulum in an attempt to produce a central dislocation. Traction applied.

7.11.45: Out of plaster, hip fixed with commencing ankylosis.

Present condition.—No recurrent infection; hip fixed; weight bearing not yet permitted.

Comment.—Response to penicillin therapy good but the treatment did not prevent destruction of the hip with ankylosis. In cases of joint involvement from the pelvis intramedullary penicillin would be impossible and it would be difficult to prevent destruction of the joint although local injections of the drug into the joint might have helped in this case to limit the arthritis.

Group 3: Formation of subperiosteal or intramedullary abscesses. In a certain proportion of cases, 7 in this series, an abscess forms in the soft parts or inside the medulla. This can be diagnosed either by fluctuation or persistent bone pain which indicates intra-osseous tension.

If the abscess is a small one it can either be aspirated or drained by a small incision and recovery is usually rapid.

If the abscess is large or tension is present in the bone then operation is indicated. In 3 cases we have drained an abscess, in 2 more the bone was also drilled. After-treatment has consisted in a light dressing with vaseline gauze, the limb being supported in a splint. At the end of a week the wound has been inspected and routine cultures have usually shown no organisms. Secondary suture has then been performed, 3 have healed perfectly but 1 has a small persistent sinus. After the secondary suture we have put 5,000 units of penicillin twice daily via a small rubber tube into the wound for five days but this is probably not essential provided that the patient is still on systemic treatment. The best time for secondary suture is from the fifth to the seventh day; if the wound is left open for a longer period suturing becomes more difficult and secondary infection is liable to occur. To those of us who were familiar with the method of repeated changing of offensive plasters it is nothing short of miraculous to see these children lying in bed with soundly healed limbs two weeks after the drainage of an acutely inflamed bone. The day of the stinking plaster has, we hope, gone for ever in this disease.

The length of time patients in this group should be immobilized depends on the radiographic evidence of the amount of bone involved. So far we have found that patients in this group do not need such prolonged rest as those in Group 2. Sufficient cases, however, have not been treated to draw any definite conclusions on this point.

One patient, an adult, was referred to the London Hospital with the diagnosis of Ewing's tumour of the femur because his pain and temperature did not respond to systemic penicillin. We were able to drain a large abscess round the shaft of the femur which relieved his pain and fever. Systemic penicillin was restarted and successful secondary suture performed in ten days' time. If an abscess is present pyrexia will not subside until the pus is let out.

CASE IV.—Girl aged 8.

Five days' fever with four days' pain in the knee.

4.8.45: Admitted in delirium with a pleural rub at both bases and swelling of the left ankle and knee. Admitted as a query rheumatic fever.

Blood culture: Heavy growth of *Staph. aureus* but unfortunately no quantitative culture performed.

Treatment.—Penicillin 100,000 units daily for eighteen days.

9.8.45: First seen in the medical ward. Knee swollen and signs of infection of the tibia. Leg immobilized.

15.8.45: Clinically improved, appetite returned but obviously a large abscess over the tibia. Knee aspirated. Fluid sterile. Large abscess drained which had burst through the periosteum. Bone drilled in two places, some pus in medullary cavity. The pus was sterile.

22.8.45: Secondary suture performed with 4,000 units penicillin solution locally twice a day for five days.

29.8.45: Stitches out, only small sinus remained.

30.8.45: X-ray showed infection upper third of tibia.

7.11.45: Completely healed with full function of knee.

January 1946: Well; walking perfectly; wound soundly healed.

Comment.—This child was severely ill with a fulminating blood infection; it is safe to say that she would have died before the introduction of penicillin. It was interesting to find the abscess when drained was sterile, and the response to secondary suture was very satisfactory.

Four of our cases had infective arthritis; the hip was infected in two of them, one developed pathological dislocation and the other became ankylosed. Diagnosis was not apparent until X-ray examination showed involvement of the joint. Local treatment consisted in a hip spica. McAdam states that intramedullary penicillin given via a needle may diffuse through the infected femur into the hip-joint; if this is so it will be a valuable aid to treatment in cases of infection of the femoral neck, but this form of therapy will not be applicable to cases of arthritis secondary to pelvic infection.

In the other 2 cases the knee was involved, diagnosis being made by finding the organisms in the joint exudate.

Treatment consisted in repeated aspiration with injection of 5,000 units of penicillin into the joint. One recovered with full function, the other has a stiff knee with commencing ankylosis.

Local penicillin will rapidly sterilize a joint but the ultimate functional result depends first on the rapidity of the diagnosis and secondly on the state of the articular cartilages after the infection has died down. Destruction of these will as a rule produce ankylosis.

CONCLUSIONS

- (1) That penicillin therapy has reduced the mortality of acute osteomyelitis from 25% to about 4%.
- (2) That if penicillin is used during the first few days of the disease complete resolution may occur.
- (3) If resolution does not occur then immobilization of the affected limb should be prolonged in those cases showing extensive bone involvement.
- (4) If operation is required secondary suture can be safely done at the end of a week. There is no longer any justification for the closed plaster treatment in this disease.

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Section for the Study of Disease in Children

President—Professor NORMAN B. CAPON, M.D.

[January 25, 1946]

Demonstration by Dr. A. W. G. Ewing and Mrs. Ewing

of the methods of ascertaining deafness and partial deafness in children under 5 years of age. Children were brought to take part in the demonstration by kind arrangement of Mr. T. E. Cawthorne and of Miss O. Beatson, headmistress of the Tottenham School for the Deaf. Audiometric tests of older children were also made.

[February 22, 1946]

DISCUSSION ON NEONATAL INFECTIONS

Dr. Beryl Corner: With some notable exceptions, paediatricians have largely devoted themselves to the problems of infancy which occur after the first two or three weeks of life. It has become increasingly clear that, since the foundations of infant health are laid in the first few weeks of life, the study of the neonatal period is of great importance, and one of the first problems that confront the paediatrician is that of neonatal infection.

In children's hospitals, infant infection is considered largely in terms of gastro-enteritis and respiratory infections, but when the neonatal period is studied, rather a different problem presents itself, since pathogenic staphylococci are responsible for so many of the lesions. When staphylococci are referred to in this paper, the coagulase test has been positive in each case.

INCIDENCE OF INFECTION

An analysis was made of 6,534 consecutive live births in two maternity units in Bristol.

The death-rate from infection in Hospital A is 0.89 per 1,000 live births, and that in B is 3.76 per 1,000 live births. Although this is not a very high mortality figure when one considers the other causes of neonatal mortality, there is a considerable incidence of infection—25.3% of all babies in Hospital A and 29.7% in Hospital B.

Eye infections account for more than twice as many cases as any other single cause. In Hospital A there is a very accurate system of records, and therefore a number of cases are included in this figure in which the eye abnormality was extremely slight and only lasted twenty-four hours, perhaps hardly warranting the term "infection". All cases where there was any discharge were swabbed and, with the exception of two gonococcal cases, *staphylococcus aureus* and diphtheroids were found. Only 89 cases occurred within the first five days of life; all the rest were in the second week. The two gonococcal cases occurred on the third day. In Hospital B three cases were gonococcal.

Staphylococcal infections of the skin are the second large group. These range from the solitary pinhead pustule to the large abscess or carbuncle. Infection of the fingers is common, but most cases were trivial. In Hospital B several cases required incision and one infant developed a tendon sheath infection and was left with a flail finger. The commonest cause of abscesses was the injection of oily vitamin K preparations. Since the use of watery vitamin K there has been no injection abscess in either hospital. Other abscesses occurred in the breasts, and subcutaneous tissues often following pustular dermatitis. Trauma from forceps was responsible for some abscesses on the scalp. In two cases areas of bone half an inch in diameter were exposed. The two carbuncles were serious infections, one being on the chin and the other on the cheek.

Mouth infections were all very slight in Hospital A; In only two cases was there any difficulty in sucking in consequence and no other constitutional symptoms. In Hospital B there were several cases with constitutional symptoms, inability to swallow and vomiting.

In Hospital A during the period under review there was quite an extensive outbreak of colds; nearly all nasal infections included occurred during this epidemic, which was undoubtedly aggravated by the fact that at the time all the infants were being taken in small baskets to an air-raid shelter with no outside ventilation. Despite this, only 27 cases of bronchitis developed in these infants. Three infants developed pneumonia in this hospital, all of whom died. One was a premature baby whose mother had started to breast-feed it and unfortunately developed a cold; one infant had a serious congenital heart lesion and caught a cold during the epidemic; the third was a normal baby who developed massive collapse of one lung on the tenth day, and died, with early bronchopneumonia found at post-mortem.

In Hospital B the incidence of bronchopneumonia is higher and fell largely on premature babies who form the bulk of the mortality figures. One child developed a staphylococcal empyema.

Only one case of diarrhoea occurred in Hospital A. This was in a 4-day-old infant whose mother had gastro-enteritis during labour. The infant responded quickly to treatment.

In Hospital B gastro-enteritis has been a considerable problem. It has occurred in numerous small outbreaks affecting most of the infants in the nursery and coinciding with gastro-enteritis in the mothers. There were 5 fatal cases, and in two outbreaks several infants required intravenous fluids. No specific organisms were isolated from stools of mothers or infants.

Suppurative arthritis of the hip-joint occurred in one infant with numerous staphylococcal skin infections.

PREVENTION OF INFECTION

From these figures it is obvious that the prevention of infection is a major problem.

In Hospital A, three or four years ago a serious effort was made to reduce infant infections. The problem was approached from the standpoint of preventing staphylococcal infection, particularly of the skin, and as a result it was found that other infections, such as gastro-enteritis, had also become much less frequent. Two factors are of paramount importance in producing lesions in the infant. First, the human carrier of staphylococci, as has been demonstrated by Knott and Blaikley, and, secondly, minute trauma to the infant's skin or mucous membranes.

As long as pustules on a newborn infant's skin are dismissed lightly as "a few septic spots", so long shall we continue to get serious or fatal staphylococcal infections in the nursery.

As a case example: an infant weighing 6 lb. 12 oz. and healthy at birth, developed a very mild conjunctivitis and a few pustules on its abdominal skin during the first week, without much attention being paid to them. During the second week weight was stationary for no apparent reason, but the child regained its birth-weight with complementary feeding. At the end of the third week the infant began to lose weight steadily, and after three days the mother took him home against medical advice. On discharge he appeared pale, but no investigations beyond test-weighing had been done. He was readmitted five days later, slightly jaundiced, with pyrexia, and having lost nearly a pound in weight. He died shortly after admission; a blood-count and rhesus compatibility tests were performed just before death and revealed no evidence of hæmolytic anaemia. Post-mortem by Professor Hewer revealed umbilical sepsis, with thrombosis of umbilical veins, focal necrosis of the liver and focal pyelonephritis, probably a blood-borne infection, all resulting from the few spots on the abdomen.

The importance of apparently trivial infections can best be brought home to the nursing staff by the keeping of accurate infant records. These may take the form of a chart, or I prefer for simplicity, a notebook in which each baby has a page for daily details of its progress and treatment; abnormalities being entered as soon as they are found. The doctor should be trained as a medical student by giving instruction in routine care of the newborn in weekly clinical rounds devoted entirely to the infants, during his midwifery clerking.

The nursing staff.—The idea is tenaciously held in many circles that the mother and baby are one inseparable unit and that the same nurse should care for both. This unit of mother and baby was the ideal in the days of private domiciliary midwifery when one nurse did all that was required for one mother and baby; but in these days of large-scale institutional midwifery, with the forty-eight-hour working week and the large number of lectures and clinics to be attended by the pupil midwife during her six months of training, insufficient emphasis has been laid by hospital authorities on the amount of time that is required for adequate care of the infants. It must be realized that, even in the smallest training units, every patient must be handled by a minimum of four nurses during the week. Thus any attempt at nursing mothers and babies in small units to imitate the domiciliary system tends to break down owing to lack of sufficient nurses.

I would urge that the babies be nursed by a completely separate nursing staff. This has the following advantages:

- (1) The nurse's whole attention is focused on the baby and thus minor lesions are readily observed and receive the maximum care.
- (2) The baby's routine is undisturbed by the maternal emergencies of the department, which are often many, and the nursery need never be left unattended.
- (3) The carrying of infection from mothers to babies is largely eliminated.
- (4) Use may be made of other types of nurses than the midwife or pupil-midwife for much of the routine work, and thus the pupil-midwife may concentrate on doing her essential work well.

Where should the baby be nursed?—Nursing with the mother in single rooms should theoretically help to prevent infection, but, since this involves a good deal more work for the nursing staff, the actual handling of the child may be carried out more roughly and quickly, with more liability to trauma and with a greater tendency to scamp details

of aseptic technique. In addition, it is more difficult for the Sister to supervise the work of pupil-midwives. At the present time it seems more practical, in large maternity departments, to nurse the infants in special nurseries, paying particular attention to details of nursing technique.

SPECIAL TECHNIQUE

In Hospital A the following details of technique have been devised:

(1) *The nursery lay-out.*—50 or more babies are all nursed in one nursery. The nursery is a long, narrow room which is partially divided into three sections. The inner part is separated from the rest of the nursery by a wall with a doorway leading into the main room. This section is the warmest part, usually being kept at a temperature of 70° to 75° F., and relatively free from draught, so that all babies spend their first three days there. They then move on to the central part of the room, where they spend their second week, going out on to the balcony whenever weather permits.

All equipment and linen for use of the babies is kept in the nursery, where all toilet and feed preparations are carried out.

(2) *Nursery staff.*—There is a special nursery staff who spend their entire time in the nursery and have no other duties. This comprises a Sister, staff midwife, one nursery trained nurse and two nursery probationers during the day, with a staff midwife and two probationers or nursing auxiliaries at night. Pupil-midwives spend a week or so of their training working in the nursery. All staff have nose and throat swabs taken and wear masks.

The nursery probationers are usually girls of 16 to 18 years of age who spend six months resident in the hospital before proceeding to nursing training in one of the other hospitals in the city, where most of them have already been accepted before coming to the Maternity Hospital. Their duties include the changing of all normal babies over 3 days old, cleaning nursery, carbolicizing, and making up of cots, preparation and clearing away of bathing apparatus, care of infants' clothes. They are invaluable members of the nursery staff, since they take over so many routine duties that the trained staff are free to care for the very young and abnormal babies. They have been found to be particularly alert about reporting slight abnormalities.

I attribute our absence of gastro-enteritis or serious skin sepsis largely to this special staff arrangement.

The babies are taken to the mothers for feeding by the ward staff and pupil-midwives who supervise all feeds.

(3) *Routine care.*—All normal infants are bathed after birth and daily from the fourth day. The bathing is done in the early morning by the staff and pupil midwives of the wards before they handle the mothers. The nurses all bath together, usually nine or ten at once, and each baths four or five babies. Each nurse has her own complete bathing outfit which she alone uses. Portable enamel baths are used which can be easily sterilised, and the nurse washes her hands in a separate bowl after undressing the baby, before starting to bath.

The bathing book is a special feature designed to check infection. The name of each pupil or staff midwife is entered daily with the names of the infants she baths. She baths the same infants and in the same order daily. Thus, if any infection occurs, it can be readily traced to a possible carrier among the nursing staff, and other babies tended by that nurse can be carefully observed.

Nursery Sister supervises bathing and trains the pupils. Ward Sisters collaborate with her closely by reading the infant report books daily and examining all babies during bathing on the tenth day and later, on the day of discharge.

After the first cleansing of eyes and mouth at birth, no routine eye, mouth or nose toilet is done. Cord powder and cotton binders are sterilized before use.

An abundant supply of easily laundered and preferably sterilizable clothing is essential, so that no soiled clothing shall remain in contact with the skin.

Since the newborn infant makes aimless wanderings of the hands and frequently scratches the face, poking the eyes and nose, the hands and arms are kept away from the face by a special form of cotton wrapper. This enables the chest to move freely and allows the baby's arms to move up and down, but not out of the wrapper. The infant has a clean wrapper at least once a day and as often as it is soiled. Septic spots on the skin frequently start as a sweat rash. No blanket ever touches the baby. Blankets spoil with frequent laundering and become harsh and tend to chafe the skin. Thus a slightly soiled blanket may be retained in use, and as it cannot be easily sterilized, may be a source of spread of infection. At birth, therefore, the baby is received in a blanket which is completely covered by a soft sheet, and a napkin is wrapped round the arms and trunk so that the infant cannot contaminate its face. In the cot, a small blanket is

enclosed in a pillow-case and this covers the infant loosely; for feeding the child is wrapped round with this pack.

Soiled napkins and clothes are placed in covered pails and after each changing these are tipped into a large bin which is kept on the fire escape outside the nursery and removed from there by the laundry staff. No soiled clothes or napkins are sluiced or washed by nurses.

In view of the danger of epidemics in such a large nursery, the slightest suspicion of infection of skin, eyes, nose, or mouth is reported at once to nursery Sister and recorded on the infant's record page. The baby is immediately barrier-nursed, and when a more severe infection is suspected, such as an impending pemphigus, gastro-enteritis or bronchitis, it is removed at once to isolation.

Barrier-nursing is performed in one corner of the nursery near the balcony. The baby is handled by the Sister or staff-midwife only. A gown is kept on the cot and always worn before handling the cot or the baby. A table reserved for the purpose is placed beside the cot and the whole screened off. All articles for toilet or treatment of the baby are kept on the table.

Further precautions that are taken to prevent infection include the barrier-nursing of all infants whose mothers have any rise in temperature, and the wearing of masks by these mothers when feeding the babies.

Following the epidemic of colds it was decided to start all infants on vitamins C, A and D on the third day, and this has been done since.

The feeding of the baby plays a considerable part in preventing infection. 85 to 90% of babies in both these hospitals are fully breast-fed on discharge, and all babies receive breast-milk only in Hospital B for the first ten days. The mortality from gastro-enteritis has been almost entirely in the hand-fed infant who has received some other food in addition to breast-milk. The greatest mortality is, of course, in the hand-fed premature baby. No epidemic of gastro-enteritis has occurred in these hospitals without there being some coincident infection in the mothers or nurses handling the babies during the period under review. In Hospital A there have been repeated epidemics of Sonne dysentery and other types of gastro-enteritis in mothers and nurses, but none among babies or nursery staff.

TREATMENT

The first point I should like to emphasize is the responsibility of nursery Sister and the great importance of isolating by barrier-nursing every infected infant, however small the infection. And, in the case of eye and skin lesions, nursery Sister should be given power to start treatment at once.

In Hospital A the infant is barrier-nursed in the nursery, unless it is a case of gastro-enteritis, pemphigus, gonococcal ophthalmia or bronchopneumonia, in which case it is removed to an isolation ward with the mother. Here mother and baby are treated as a domiciliary case and one or two nurses only do full-time duty, gloves as well as gown being worn whenever the infant is handled.

In treatment of skin lesions it is important to isolate the lesion from the rest of the infant's skin, and therefore dressings should be used to cover the spot, and whenever it is uncovered the clothes and surrounding skin should be protected by a dressing towel. One so frequently sees septic spots on the head, for instance, being rubbed against the sheet and thus contaminating other areas of skin.

The application I have found most useful for skin lesions has been a paste of 5% sulphathiazole in glycerine. This is applied to the lesion every time the infant is fed or changed and the majority of pustules will clear in twenty-four to forty-eight hours if this is carried out conscientiously. In the one case of pemphigus in Hospital A, no fresh lesions were present after forty-eight hours and the skin was healed in five days.

Penicillin cream, 400 units/gramme Lanette wax, has been used in 31 infants with pustular dermatitis or superficial skin lesions. When applied three-hourly it cleared the skin slightly more quickly than the sulphathiazole paste. In several patients, with a number of lesions of the same date, both these pastes were applied three-hourly and the skin cleared equally quickly. This was tried in two cases of pemphigus. The main superiority of penicillin was shown in dealing with abscesses. The two carbuncles each cleared in three days with local application only, and for other abscesses the pus was aspirated and penicillin injected once daily into the cavity. This was used in 11 abscesses, the average number of injections required being three. In 3 cases, intramuscular penicillin was given as well in large doses, twice daily, until the abscess had localized. This treatment avoided incision and constant dressings afterwards.

For more serious infections the use of penicillin appears to be a considerable advance. Pneumonia, fortunately, has been uncommon in my series of cases, but 12 cases have

been treated with penicillin with 3 deaths, all in premature infants. Oxygen tents were used in every case, and sulphathiazole in addition in these three fatal cases.

The following severe cases illustrate the use of penicillin:

One baby developed pneumonia towards the end of its second week, during an epidemic from which three deaths occurred. Six days later it had physical signs suggesting an empyema, and on aspiration thick pus was withdrawn which grew pure culture of *Staphylococcus aureus*. There was also a bronchial fistula. This infant was given intensive systemic penicillin, 20,000 units daily, for fourteen days, and rib resection and drainage were done. It has made a satisfactory recovery.

Another similar case occurred during the fourth week of life in another hospital. Again penicillin intramuscularly was given for two weeks, followed by rib resection and drainage. Complete recovery occurred and the lung fully expanded. This infant is now aged 9 months and has a completely expanded normal chest.

The third instructive case was a premature baby weighing 3½ lb. who developed severe pneumonia on its thirteenth day. It was placed in an oxygen tent and penicillin, 24,000 units daily, by three-hourly injections, was given for twenty-one days until the temperature became normal. A full course of sulphathiazole for five days was also given during this time but made no appreciable difference to the clinical condition or temperature. Oesophageal feeds were given for two weeks and the infant ultimately made a satisfactory recovery. It was fed almost entirely on breast-milk throughout.

The last example of penicillin treatment is the baby with suppurative arthritis.

This infant weighed just under 5 lb. at birth. It developed jaundice due to hæmolytic disease of the newborn during its first few days. On the seventh day a large ulcer appeared inside the upper lip, from which *Staphylococcus aureus* in pure culture was grown. At the same time a whitlow appeared on one finger. The child's condition was poor, although it had previously been transfused, and therefore systemic penicillin was started, 5,000 units daily, by four-hourly injection intramuscularly. The mouth cleared in a few days and the finger was incised. It was in the early days of penicillin and, as the oral swab was negative, the supply of penicillin was stopped. The infant remained feeble, too weak to breast-feed, transfusion wounds then became infected, septic spots appeared on the umbilicus and abdomen. Slight pyrexia continued. About ten days later swelling of the right hip region was noticed, and aspiration withdrew 20 c.c. of pus, pure culture *Staphylococcus aureus*. An X-ray showed intensive involvement of the hip-joint, with osteomyelitis of the upper end of the femur. Daily aspiration and injection of penicillin solution, 500 units/c.c. was then done for ten days, at the end of which time no further pus could be aspirated. The infant left hospital at the end of five weeks, fully breast-fed and thriving. There was a little shortening of the affected leg, and about 75% range of movement was present in the hip-joint.

REFERENCE

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Total No. of babies	3,344	3,190
No. of infected babies	869 (25.9%)	949 (29.7%)
No. with more than 1 type of infection	83 (9.5%)	129 (13.5%)
No. with more than 2 types of infection	8 (0.9%)	33 (3.4%)
Deaths from infection	3 = 0.89 per 1,000 live births	12 = 3.76 per 1,000 live births
Superficial skin lesions including paronychia, other whitlows, styes	193 { Cuticles 69 Whitlows 4 Styes 5	265 { Spots 213 Whitlows 1 and cuticles 45 Styes 7
Umbilical infections	4	20
Subcutaneous abscesses, ... boils, infected forceps wounds...	21 (Infected forceps 7)	48
Carbuncles	—	2
Pemphigus	1	4
Eye infections	451	563
Mouth infections	45	61
Nasal infections	191	68
Otitis media	1	6
Bronchitis	27	18
Pneumonia	3	17
Empyema	—	1
Gastro-enteritis	1	40
Urinary infections	2	7
Joint infections	0	1

Professor Arnold Sorsby: *Ophthalmic aspect [Abstract]*.—The incidence of blindness in children aged 5 to 16 years has declined in England and Wales from 36.4 per 100,000 in 1923 to 28.8 in 1933, and 20.3 in 1943. The considerable diminution in infectious disease in childhood is responsible for this decline. The incidence of blindness from phlyctenular ophthalmia and congenital syphilis has gone down considerably, but the most significant reduction has been in blindness from ophthalmia neonatorum. In 1922, 30.4% of all children at blind schools had been blinded by ophthalmia neonatorum. In 1944 the incidence had declined to 9.2%. At the present some 67% of all children at blind schools have been blinded by congenital anomalies including myopia. These congenital anomalies are probably in the main genetic affections, but an unknown proportion are caused by transmitted maternal infections. It is now clear that apart from congenital

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Professor Arnold Sorsby: *Ophthalmic aspect [Abstract]*.—The incidence of blindness in children aged 5 to 16 years has declined in England and Wales from 36.4 per 100,000 in 1923 to 28.8 in 1933, and 20.3 in 1943. The considerable diminution in infectious disease in childhood is responsible for this decline. The incidence of blindness from phlyctenular ophthalmia and congenital syphilis has gone down considerably, but the most significant reduction has been in blindness from ophthalmia neonatorum. In 1922, 30.4% of all children at blind schools had been blinded by ophthalmia neonatorum. In 1944 the incidence had declined to 9.2%. At the present some 67% of all children at blind schools have been blinded by congenital anomalies including myopia. These congenital anomalies are probably in the main genetic affections, but an unknown proportion are caused by transmitted maternal infections. It is now clear that apart from congenital

syphilis, toxoplasmosis and German measles in the mother can produce extensive ocular lesions in the offspring. Whooping-cough may also be a factor.

The most clearly recognised neonatal infection is ophthalmia neonatorum. There is no reason for assuming that ophthalmia neonatorum itself has declined to any extent, but the reduction in the incidence of impaired vision and blindness from ophthalmia neonatorum is brought out by the following typical rates per 100,000 births:

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Statutory notification, introduced in 1914, together with the provision for necessary treatment, must be regarded as the main cause for the gratifying decline in the incidence of impaired vision and blindness. It is not certain that the use of prophylactic drops, which is part of the Credé procedure, is a significant factor, but it would appear that the organic silver preparations are as effective as silver nitrate itself. General sulphonamide therapy has revolutionized the treatment of ophthalmia neonatorum. Clinical cure can be obtained within three days in some 30% of cases, whilst over 80% have recovered within eight days. Of the sulphonamides sulphamezathene is the most generally useful. Even better results can be obtained by the local use of penicillin. Frequent applications in adequate concentration are essential. Cure in most cases can be achieved within a matter of hours.

Ophthalmia neonatorum to-day is not mainly gonococcal infection. Only some 25% of cases are gonococcal. At least 10% are caused by a virus, which is responsible for a *virüs cervicitis* in the mother. The staphylococcus is the commonest organism being responsible for some 35% of cases, but many other organisms are found. Both bacterial and virus ophthalmia neonatorum respond readily to the sulphonamides and to penicillin. Though the complications of ophthalmia neonatorum are now well under control, there is still much to be done in eliminating the affection itself. Essentially this is a problem of ante-natal care.

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Dr. Field therefore decided to try prophylactic swabbing of the babies from birth with a similar CTAB solution as well as a series using penicillin cream (*see below*). There

Penicillin Cream		Cetyl Trimethyl Ammonium Bromide (CTAB)	
Lanette wax S.X.	2½ ounces	Arachis oil	4
Paraff. melle flav.	1 ounce	Celofas W.F.Z.	1.25
Arachis oil	3 ounces	Boric acid	2.0
Buffer solution	2½ ounces	CTAB	0.2 (later reduced to 0.1)
Distilled water	to 1 gallon	Water	to 100.0
with chlorocresol	35 grains		
Sterilized by autoclave then penicillin solution added daily as required to make 200 units per ml.		Sterilized by autoclave.	

are about a thousand deliveries a year at the hospital and the babies are nursed in four nurseries, each containing approximately ten babies. Nurseries A and B are on the same floor with the same nursing staff, nurseries C and D are on different floors with different nursing staff. In nursery A the babies were swabbed all over from birth daily with penicillin cream, nursery B was used as a control, the babies being washed daily as usual. In nursery C babies were swabbed with CTAB solution and nursery D was used as a control with daily washings. The investigation has been in progress for about a year during which time the nursing staff have been instructed to report any pustule or inflammation of the skin; sore buttocks have not been included.

RESULTS

Nursery A (Penicillin cream)—No infections.

Nursery B (Control)—Three infants with infections—Mild.

Nursery D (Control)—Five infants with infections—Mild.

Nursery C (CTAB for nine months)—Eight infants with infections—some severe. (Penicillin for three months)—No infections.

In nursery C Sister reported that the CTAB appeared to irritate the skin so penicillin cream was tried instead and no infections have since been reported.

REFERENCE

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Section of Comparative Medicine

President—W. A. Pool, M.R.C.V.S.

[February 20, 1946]

DISCUSSION: INTESTINAL DISORDERS OF THE NEWBORN

Dr. Robert Cruickshank: I shall discuss only the *diarrhoeal* disorders of the newborn and include, for the sake of comparison data on the enteritis of infants past the neonatal period. There are three main points which I should like to put forward: (1) That the infant is prone to infection with endogenous bacteria; (2) that such infection is facilitated by adverse environment; and (3) that the infant is ill-adapted physiologically and immunologically to deal with infection.

(1) *Endogenous infection*.—By endogenous bacteria is meant those organisms—staphylococci, pneumococci, monilia, coliform bacteria—which very early in life become resident on the skin, in the nose and upper respiratory tract and in the intestine, and which in the older healthy child have little power to invade or infect. *Staphylococcus aureus* is present in the nose of 80% to 100% of babies in the first few weeks of life and is responsible for most of the mild infections of conjunctiva and skin which are so frequent in the neonatal period (outbreaks of pemphigus neonatorum may be due to more virulent "epidemic" strains of the staphylococcus). From these localized infections dissemination to deeper tissues may occur, causing pneumonia, osteomyelitis, or septicæmia, with serious consequences for the infant. Sometimes *Staphylococcus albus* is isolated from the blood in such numbers as to indicate that it, too, may produce generalized infection in the susceptible infant. Pneumococci are present in the upper respiratory tract of 30% to 60% of infants and certain types (for example 4, 6, 19 and 23) predominate in the early period of life. These are the types which are also most frequently isolated from infants with pneumococcal infection (otitis media, bronchitis and bronchopneumonia) and one or two of these types may predominate in an infected community (Hendry, 1942). Thrush is an infection which is more frequent in early infancy than is usually realized. Clinical infections have been shown to occur in 4% to 5% of infants in the first ten days of life, and can cause considerable upset in the neonatal period by interfering with feeding; when the infection extends to the œsophagus and stomach, more severe symptoms, e.g. anorexia, blood-stained vomiting and even death, may follow. Both latent and clinical infections are three to four times more frequent among artificially-fed than among breast-fed babies, probably associated with the greater risk of contact infection from bottles, teats, nurses' hands and the like (Ludlam and Henderson, 1942). Spread of these potentially pathogenic bacteria is facilitated by propinquity and overcrowding, so that in the case of an organism with a multiplicity of types one or two particular types may be isolated from a group of children who are in close contact with each other. When through adverse environment infections occur, these particular types will be found to be responsible for the lesions and may give the impression that the infection was due to an "epidemic" strain of the organism.

When infantile diarrhoea is considered in the light of these findings it at once becomes noteworthy that this disease is much more frequent and more severe in artificially-fed than in naturally-fed babies, in-common with a high content of coliform bacteria in the intestine of the artificially-fed child and their rarity in the bowel of the breast-fed baby. Thus, in an outbreak of neonatal diarrhoea in a maternity unit where at the time only 12 of 30 babies were wholly breast-fed, these 12 babies alone escaped infection; the remaining 18 all developed diarrhoea and all died (Sakula, 1943). In another outbreak (Ormiston, 1941), the fatality rate among the breast-fed infants was 14% and among those artificially-fed 60%. Similarly in gastroenteritis of older infants only 5% to 10% of the cases occur among breast-fed children, and breast-feeding even for a few weeks seems to give the baby an added resistance in overcoming infection (Gairdner, 1945). That certain Gram-negative coliform organisms may be especially incriminated in the causation of infantile enteritis is suggested by the early work on summer diarrhoea by Morgan and Metchnikoff, both of whom reported a high incidence of proteus types. Lately Sakula has found *Ps. pyocyanea* unusually common in cases of neonatal diarrhoea, and Bray (1945) reported the recovery of *Bact. neapolitanum* from over 90% of cases of gastro-enteritis in older infants. Obviously, a reliable classification of the coliform group, either serologically or by phage typing, is needed to determine whether specific types have, like certain pneumococcus types, the capacity to spread and to initiate infection when resistance is lowered. Progress towards this end was made by the early work of Kauffmann and lately by Vahne (1945) who

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are about a thousand deliveries a year at the hospital and the babies are nursed in four nurseries, each containing approximately ten babies. Nurseries A and B are on the same floor with the same nursing staff, nurseries C and D are on different floors with different nursing staff. In nursery A the babies were swabbed all over from birth daily with penicillin cream, nursery B was used as a control, the babies being washed daily as usual. In nursery C babies were swabbed with CTAB solution and nursery D was used as a control with daily washings. The investigation has been in progress for about a year during which time the nursing staff have been instructed to report any pustule or inflammation of the skin; sore buttocks have not been included.

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lack is in the capacity to produce new antibody which, recent research indicates, may be derived principally from the lymphocytes, and the great lymphocytic activity in the first few years of life is probably an indication of the infant's efforts to make good this deficiency. The resistance of the breast-fed child to endogenous infection raises the question as to whether it derives maternal antibody through suckling. Objective evidence is mostly negative. Human colostrum, unlike that of sheep or cow, is low in antibody-content and there is no increase of diphtheria antitoxin in the infant's blood as a result of suckling (Kuttner and Ratner, 1923). Yet, Gröer and Kassowitz (1919) claimed that diphtheria antitoxin persists longer in the blood of the breast-fed than of the artificially-fed child, and clinical experience suggests that breast feeding gives the infant a greater resistance to infections, e.g. bronchopneumonia, other than enteritis. This is a matter for further study. Meanwhile it may be claimed that in the present social conditions breast feeding by 80% of mothers for six months—surely an attainable objective—would materially reduce the mortality from infantile enteritis.

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Dr. R. Lovell: The intensive breeding of domesticated animals and the unnatural methods of rearing and feeding which are necessary because of economic conditions take a heavy toll of the newly born. The infective agents which cause the actual death of the animals are often of low pathogenicity and even harmless in adult stock. These agents assume a pathogenic rôle when the delicately balanced equilibrium which a newly born animal has to establish with the outside world is upset. This equilibrium is easily upset when modern economic conditions have a tendency to interfere with the normal processes of nature. One example may be taken from the dairy industry whereby calves are removed from the mother at birth so that more milk may be available for human use. It is therefore necessary to consider the probability that not one but a multiplicity of causes are frequently involved in these diseases. Diseases of the newborn thus may not always be introduced from outside but often result from an upset in the balance established between an animal host and the prevalent bacteria. I have selected two of the common, well-known disorders of young stock for the introduction to this discussion, lamb dysentery, and white scours of calves.

Lamb dysentery.—This is a well-known disease of young lambs which is frequently fatal and has been recognized for many years in certain areas in the Border Counties of Scotland and England. It is now known to exist in very much wider areas and occurs not only in Great Britain but also in other parts of the world. Lambs up to one week of age are most often affected but it has been found in lambs up to about three weeks old. Infection appears to be by ingestion of *Clostridium welchii* type B, and the specific lesions are found in the intestine and vary from small discrete ulcers to large areas of necrosis of the wall of the intestine. At the beginning of an outbreak a few of the newborn lambs only may be infected, but there is often some apparent increase in the virulence of the organism and there is a higher frequency of the disease in lambs born later in the year. On the other hand this may be associated with a greater weight of infection.

It is well known that *Cl. welchii* type B is a toxin-producing organism and that treatment of lambs is not practicable. Two methods of prophylaxis are available: (1) Vaccination of the ewe. The vaccine consists of a formalinized culture of the causal organism and ewes are injected during the autumn and again about ten days before lambing is due to begin. The ewe thereby obtains an active immunity and antibodies are transmitted to the lamb by the ingesting of colostrum. The mucous membrane of the intestinal tract of the lamb is permeable to these antibodies for the first few days of its life, and the lamb is protected during the susceptible period.

(2) Lambs may be injected within a few hours of birth with lamb dysentery serum prepared in horses and a passive immunity is thereby induced by artificial means in the lamb; but this method of prophylaxis is not as practicable as vaccination of the ewe.

Although that is briefly the story of lamb dysentery it is as well to remember that there are causes which predispose to the disease, and these were more freely discussed when the aetiology of lamb dysentery was obscure. Lambs which suck well and overload themselves with milk appear to develop the disease more often than those

has subdivided the coliform group into some 115 types on the basis of O (somatic), K (capsular) and H (flagellar) antigenic analysis. Vahlne found a high incidence of two or three groups among coliform strains isolated from cases of cystitis, appendicitis and cholecystitis, and so it may be that certain coliform organisms will come to be recognized as more potentially pathogenic than others.

Another common organism in the intestinal flora of the artificially-fed baby is *Str. faecalis* or the enterococcus. In this connexion there may be significance in the work of Gale (1944) who found that some strains of *Str. faecalis* were active producers of tyramine from tyrosine, and that tyramine was toxic to young rats which had not yet developed a specific detoxicating enzyme. Babies in the first few months of life also lack this enzyme, and as active tyramine-producing strains of *Str. faecalis* have been found in the stools of babies with neonatal diarrhoea, it was suggested that these organisms may be causally related to the condition. My colleague Mrs. Helen Tomlinson (*née* Epps) has followed up this promising inquiry by examining the enzymic activities of a large series of coliform organisms from babies with diarrhoea and from normal cases, but so far has found no evidence of the production of toxic amines similar to those produced by the enterococcus.

No discussion of the aetiology of infantile enteritis would be complete without reference to the viruses. Two claims have been made for the isolation of a virus-like agent from infants with diarrhoea. Light and Hodes (1943) were able to induce diarrhoea in calves with filtrates of faeces from cases of neonatal diarrhoea. The causative agent was peculiar in that it could withstand heat at 100°C. for five minutes and the possibility that a natural virus of calves was being activated could not be ruled out. Buddingh and Dodd (1944) have described a syndrome of stomatitis and diarrhoea in infants from whose mouth lesions a virus-like agent was isolated, but the syndrome does not correspond with the usual type of gastro-enteritis seen in this country. Another infection characterized by nausea, vomiting and profuse watery diarrhoea has lately become prevalent in certain communities in this country, and while primarily an infection of adults, may affect babies in a maternity unit. The infection may attack breast-fed as readily as artificially-fed babies but is, as a rule, mild and the case mortality is low (Brown *et al.*, 1945).

(2) *Adverse environment.*—It is generally accepted that poor environment increases both morbidity and mortality from infantile enteritis. A few examples must suffice. Gastro-enteritis is predominantly a disease of poor-class urban areas. Thus, in the Royal Borough of Kensington, deaths from enteritis in 1933 were thirteen times more frequent in the poor northern district than in the wealthy southern area. Again, illegitimate infants deprived of parental care have a high mortality rate from gastro-enteritis, and in London the illegitimate child has a one in forty chance of dying from diarrhoea before it reaches its first birthday. Institutional care also increases the risk of diarrhoea, and the unique finding of a rising mortality rate from gastro-enteritis since 1930 in Greater London in contrast to other county boroughs may be related to the large numbers of infants admitted to hospitals and institutions in the London area. The increase in deaths from infantile enteritis in the war years and the occurrence of large-scale epidemics in some of our cities may be a reflex of the lower hygienic standards during the war.

(3) *The infant's defence against infection.*—The human infant must not be regarded as a miniature man. Its physiology is still immature and may be easily upset. For example, gastric acidity is low in the first few months of life and only reaches adult level by the end of the first year. Cow's milk curd is less easily digested than human milk and needs a greater amount of gastric juice. This fact, and the greater amount of base in cow's milk, may account for the alkaline reaction of the intestinal contents of the artificially-fed child. As a result the upper reaches of the gut may be colonized by coliform bacteria which in this way act as an irritant to the bowel. Further, toxic products of bacterial growth may be absorbed to the liver which often shows evidence of toxic damage in gastro-enteritis. Again, the infantile kidney has a poor excretory function, particularly for waste products and sodium. With excess fluid loss by the bowel, urea is retained in the tissue; oedema may follow, respiration is embarrassed, and anoxaemia may contribute to a fatal issue.

When infection occurs, the body tissues ordinarily react by an outpouring of phagocytes followed by the production of specific antibodies. The newborn infant with inadequate material in the shape of low plasma protein, poor plant in the form of an undeveloped lymphatic system, and unskilled workers stimulated by immature polymorphonuclear and monocytic cells, is ill-adapted to cope with bacterial invasion. The fraction of the plasma protein most important for defence against infection is the globulin in which antibody is contained, and it is known that the newborn lamb or calf, dependent on colostrum for its maternal antibody, has a low globulin content. The human infant, on the other hand, receives maternal antibody through the placenta, and should have adequate globulin at birth although there are but scanty data on this point. Its main

On the other hand these seasonal changes may be associated with a lack of vitamin D. It has been pointed out that sunlight during the summer and autumn may provide the calf born during the autumn with more vitamin D than the spring calf can obtain, and a lack of this vitamin may be as important as vitamin A. The seasonal changes may of course be associated with the character of the milk curd found in the stomach of the calf, and the milk of stall-fed cows is possibly not so easily dealt with by the calf as is milk from cows which have been at pasture.

Although white scours of calves is assumed to be one of the intestinal disorders of the newborn, it must be emphasized that most cases examined post-mortem show the presence of *Bact. coli* or some similar organism in the blood-stream. The disease is therefore a septicæmia and an antigenic substance obtained from strains of *Bact. coli* by chemical extraction is lethal to calves when given intravenously. This substance has been extracted from mucoid strains of *Bact. coli* and is capable of producing toxic symptoms in mice, manifested by diarrhœa and rapid breathing; a toxic effect can also be demonstrated in rabbits and in some cases is associated with diarrhœa. This substance will apparently induce the formation of antibodies to itself as shown by precipitation, but the serum antibody does not appear to be capable of protecting experimental animals from the toxic manifestation. A similar substance is also present in strains of *Proteus vulgaris* and *Ps. pyocyanea*. Although the work is very incomplete and no conclusions can be reached, it does serve to indicate that white scours of calves is not necessarily a specific intestinal disorder, but that the scouring is probably a manifestation of a general disease. Investigations of this kind may not explain or help towards a fuller understanding of the ætiology of white scours but will perhaps indicate the reasons why calves die when infection develops. It is of course possible that *Bact. coli* may not be of such importance as we believe, and it must be remembered that some of the early workers on lamb dysentery recovered *Bact. coli* from diseased lambs, and the significance of this organism was not clear at the time.

There are many gaps in our knowledge of these diseases of the newborn and those who have opportunities to observe the natural history of such diseases should note and record their observations. I believe that such an approach to the problems will give invaluable guidance and help to the experimentalist who is expected to solve problems and so often fails.

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Professor A. N. Worden referred briefly to certain as yet unpublished experiments on newborn calves which had been commenced during 1943 by F. Blakemore, T. Moore, himself and others at Cambridge (vide *Proc. R. Soc. Med.*, 1944, **37**, 446) and discussed them in relation to the earlier work of Theobald Smith, R. B. Little, Marion L. Orcutt, Paul Howe and their collaborators (*J. biol. Chem.*, 1921, **49**, 109 and 115; *J. exp. Med.*, 1922, **35**, 161; 1925, **41**, 81, 89 and 413) and to naturally occurring cases of disease in newborn calves. He still felt that experimental work on human cord bloods as reported by G. L. Boyd (*Canad. med. Ass. J.*, 1922, **12**, 274) and by J. H. Lewis and H. G. Wells (*J. Amer. med. Ass.*, 1922, **78**, 863) should be repeated with the aid of modern biochemical techniques.

Dr. R. L. Worrall agreed with Dr. Lovell that infectious diarrhœa of the newborn was a general disease. Enteritis was a misnomer, in view of the frequent absence of intestinal inflammation in infants dying from diarrhœa and vomiting. The disease was most prevalent in warmer weather and in hot climates. This would seem to suggest bacterial rather than virus causation if the infection was food- or water-borne. In attempting to distinguish particular strains of *B. coli* as possible infectious agents, bacteriophage typing rather than serological typing might prove more successful. Therapeutic administration of gamma globulin would be worth trying.

Dr. Robert Sutherland: It is perhaps unwise to apply the term *endogenous* to infections in the newborn infant, as this implies inevitability. The organisms concerned must have reached the infant from outside sources and an attempt should be made to limit the assaults made upon his imperfect antibody mechanism. The child probably has a high resistance to infections by organisms living in non-pathogenic association with his mother. The mother and her child should therefore be regarded as a mother-child unit and every care should be taken to protect the infant from organisms from other sources. We must also try to improve the newborn infant's resistance to infection. It may be that a general improvement in the health and nutrition of pregnant women would lead to improved powers of phagocytosis and antibody formation in their infants. It would be interesting to get a comparative study of these powers in infants born to women in income-groups I and V.

which appear to be less greedy; and this is bound up with an abundance of milk in the ewe and this in turn is influenced by the good condition of the grass. Handling of lambs by the shepherds no doubt helps to spread the disease in infected areas and the suckling of lambs by ewes which have lost their own has a similar influence. The breed of sheep is also of importance and cross-bred lambs are apparently less susceptible than some of the pure-bred ones.

These well-known observations are worth considering when discussing similar conditions of the newborn, the ætiology of which is still far from clear.

White scours in calves.—This is considered to be one of the common diseases of calves and attacks them within a few hours or days of birth. It has a seasonal variation, there being a higher mortality in calves born in the spring than those born in the autumn, and is in most cases associated with invasion of the blood-stream by *Bact. coli* special virulent strains of which exist; predisposing causes are, however, apparently necessary. It is difficult to estimate how common this disease is but a survey made in 1936-37 showed that in well-managed herds in this country there is a death-rate in calves of about 5.5% (Lovell and Hill, 1940). If we accept as a rough estimate that there are in England and Wales three million cows and heifers in milk, cows in calf but not in milk, and heifers in calf, and if we assume that the birth-rate is two thirds of this, then some two million calves are born in England and Wales per year. The number which die will be at least 110,000 and it was shown some years ago (Lovell and Hughes, 1935) that 37 of 100 calves which died succumbed to white scours. A simple calculation based on these figures shows that there is an annual loss of over 40,000 calves from white scours in England and Wales. Although this is a high figure it is probably a conservative estimate.

Bact. coli is accepted as the common organism associated with this disease in calves, and the predisposing causes are probably associated with inadequate digestive functions, lack of colostrum or over-distension of the digestive tract. Colostrum supplies the calf with certain proteins—globulins—and there is a relationship between the accumulation of globulins and the appearance of antibodies in the blood of calves following the feeding of colostrum. It is clear that colostrum has at least one function, which is to provide calves with antibodies against prevalent bacteria which are harmless to them in later life. These antibodies are in a higher concentration in the colostrum than in the serum and the intestinal wall of the newborn calf is permeable to these antibodies for the first two to three days of its life. It has been shown by American workers that a protective meal of serum from a cow in the same environment will also protect calves but apparently less effectively than colostrum. On the other hand some observers suggest that colostrum acts because of its vitamin content and that calves born of mothers with a low content of vitamin A in the colostrum are more liable to infections such as white scours than calves born of mothers whose colostrum has a higher vitamin A content. Attempts have been made to influence the incidence of white scours by giving vitamin A concentrates at birth. Attention has also been paid to other vitamins, for the synthesis of the B complex may be inadequate in the newborn calf; where colostrum is likely to be deficient or where scouring exists, the giving of shark-liver oil and capsules containing one or more of the B group of vitamins has been recommended.

No one doubts the value of colostrum to the newborn but wherein does this value lie? Is it the antibody content? It may be, but it may be that the vitamins or even the protein which colostrum supplies help the calf in its resistance to disease.

There is undoubtedly a delicate balance existing between *Bact. coli* and the intestinal tract of calves and although the lack or deficiency of colostrum may be one of the causes which upset that balance in favour of the bacteria, the intestinal disturbance may be induced by infrequent feeding or feeding too much at a time. It is generally conceded that suckled calves do better than bucket-fed ones and losses are negligible in calves suckled on nurse cows for the first month or so of life. Preventive measures and investigation should therefore be directed also towards the general conditions under which calves are born and reared. This implies the paying of attention to the mother, for the seasonal swing in mortality of calves has been linked up with the diet of the mother during the later days of pregnancy. It has been concluded that as the cow stores vitamin A while at pasture and loses it during the winter, then a winter pregnancy is followed by a low vitamin A content of the colostrum in the spring months of the year. Attempts have been made to increase the vitamin A content of colostrum by feeding carrots and cod-liver oil to cows during the later months of pregnancy and suggestions have been made that cows should be allowed a non-lactating period of not less than three months in order to ensure a high vitamin A content of the colostrum. It must be remembered that cows are expected to secrete enormous quantities of milk and to nourish a fœtus at the same time; good calf husbandry must therefore be linked with care of the mother during pregnancy.

Section of Anæsthetics

President—GEORGE EDWARDS, M.R.C.S., D.A.

[February 1, 1946]

DISCUSSION ON ANÆSTHETICS IN TROPICAL CLIMATES

Dr. H. K. Ashworth: The title "tropical climates" does not imply conditions of heat limited only to the geographical boundaries of the tropics. Many parts of the world outside these geographical limits provide similar climatic problems for the anæsthetist. In addition there is another factor besides that of heat, namely the effect of high altitudes on the administration of anæsthesia. The ideal remedy for the majority of climatic difficulties in the tropics is, of course, a properly air-conditioned operation theatre block, including resuscitation and recovery rooms, and efficient cold storage for drugs. The use of an air-conditioned operation theatre block has been criticized on the grounds that the eventual transfer of the patient to less temperate conditions is prone to increase the incidence of post-operative pulmonary complications. Unfortunately, no comparative figures are available from which to draw an accurate conclusion as to the validity of this criticism. What is certain, however, is that the pulmonary morbidity would require to be a big factor to outweigh the proven advantages of air-conditioning, which are as follows:

- (1) Avoidance of dehydration of the patient by minimizing the otherwise excessive sweating during anæsthesia.
- (2) Minimization of the excessive heat factor which often predisposes to the development of ether convulsions.
- (3) Provision of less exhausting conditions for the operation theatre personnel.
- (4) Provision of fly-proof and dust-proof conditions in the operation theatre.

Air-conditioned theatre blocks are unfortunately expensive to erect and maintain and although the ideal, one is unable to visualize their installation in the immediate future in more than a small percentage of the total number of operation theatres in the tropics. This being the case, it is necessary to consider the effects of lack of air-conditioning on anæsthesia in hot climates.

Equipment and drugs.—(1) Whatever apparatus is used, the more vulnerable parts should be duplicated. The best machine is useless if it has to stand idle while a replacement is obtained from England. A water sight-feed Boyle's apparatus may not enable the anæsthetist to command the full range of inhalational anæsthesia, but at least it has the advantage of relative invulnerability to rough handling by native theatre orderlies and ease of repair in case of damage.

(2) If CO₂ absorption is used, it is recommended that the apparatus should be fitted with a circle rather than a "to and fro" absorber, as it was found that a canister at the face-piece soon became unpleasantly hot, and it was felt that such a state of affairs, if prolonged, would be detrimental to the patient.

Hot, dry climates provide the optimum conditions for the accumulation of static electricity and the usual precautions as to earthing of apparatus, moistening of rubber parts, avoidance of friction, and of short-circuits of electrical instruments are absolutely essential in such climates.

Medical gas cylinders may only be filled to 90% of their normal stated capacity in British tropical possessions. Ether should be supplied in tins and not in bottles—the waste by evaporation even from unopened bottles was colossal.

One frequently heard that it was impossible to induce or to keep a patient sufficiently anæsthetized with open ether in hot climates, but this was soon disproved.

Dr. Cruickshank has shown conclusively the vital importance of breast-feeding. Our complacent acceptance of artificial feeding in 80% to 90% of 1-month old babies and 50% of 4-month old babies is something of which we should be ashamed. Doctors and nurses must realize their grave responsibility in this matter. We should feel that it is a reflection upon us if a baby in our charge is deprived of these advantages. Tied up with this, it is essential that doctors and nurses should learn more about the difficulties of breast-feeding and how to deal with them. Failure to insist upon the continuation of breast-feeding is often due to lack of knowledge of how to make it possible; recourse to artificial feeding is the easiest way out of a difficult situation. The better education of the profession in the problems of infant feeding and handling is therefore an essential corollary to a public campaign in favour of breast-feeding.

Dr. M. Dynski-Klein endorsed Dr. Cruickshank's views on the potential pathogenic importance of endogenous *Bact. coli* in the genesis of intestinal disorders of the newborn. Clinical studies carried out in the University Children's Clinic in Prague (Profs. Fischl, Epstein) in order to determine the nutritive value of expressed breast-milk showed that 50% of babies fed this milk did not develop the Gram-positive (*Lacto bacillus bifidus*) flora ("Blue bacillosis") of the breast-fed infant, but instead showed the Gram-negative coli flora ("Red bacillosis") found in artificially-fed infants. Changes in the pH of the faeces preceded the appearance of *Bact. coli*. Infants fed the expressed breast-milk developing a *Bact. coli* flora failed to thrive and sooner or later showed gastro-intestinal disturbances of varying severity. Feeding sterilized breast-milk gave the same result. Addition of carbohydrates not readily fermented, such as rusk flour or 5% to 7% rice gruel, to expressed breast-milk favoured development of the bifidus flora and once this had been established the infants started to gain weight and gastro-intestinal symptoms disappeared. It thus seems clear that, in addition to exogenous infection, gastro-intestinal disorders may be brought about by any diet favouring the growth of *Bact. coli*. This may be caused by changes in the composition of the intestinal chymus. Breast-feeding is thus the strongest weapon in the prophylaxis of gastro-enteritis in the newborn and repeated outbreaks of this disease in the Maternity Department of the West Middlesex County Hospital have been successfully controlled by raising the rate of breast-feeding to 98%. The amount of diphtheria antibody transmitted through breast-feeding is insignificant and active immunization of mothers is thus of no value for passive immunization of infants against disease.

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Mr. M. Crawford said that Dr. Cruickshank had alluded to the possibility of a virus being concerned in the aetiology of gastro-enteritis and had asked if any member with veterinary experience had any knowledge of the behaviour of the foot-and-mouth disease viruses in young calves. He had seen many outbreaks of foot-and-mouth disease in dairy herds in Ceylon, a country in which the slaughter policy was not enforced. A feature of these outbreaks had been a number of sudden deaths in young suckling calves. These had not shown the usual symptoms and lesions of foot-and-mouth disease. Calves, to all appearances healthy, cried out, fell to the ground, struggled violently for a short time and died. On post-mortem examination a most intense reddening of the gastric (4th stomach) and intestinal mucous membranes was present. The appearances resembled that seen in acute irritant poisoning such as acute arsenical poisoning. Such deaths occurred only at times when foot-and-mouth disease was rife in the herd. Another virus disease which Mr. Crawford had observed in calves was cowpox. That disease occurred frequently in Ceylon in milch cows. Calves suckling infected cows usually developed pock lesions in the mouth, the lesions being surrounded by a generalized inflammation of the buccal mucous membrane. They lost condition and suffered from diarrhoea. It was not possible to say whether lesions of gastro-enteritis were present or not as opportunity for post-mortem examination had not occurred.

Dr. Martin Bodian discussed the incidence of positive blood cultures mentioned by previous speakers in connection with gastro-enteritis in newborn human beings and animals—one speaker had even mentioned four blood cultures taken on successive days from a sheep, and positive for four different organisms.

Dr. Bodian drew attention to his own early results in neonates with a fair number of strains of *Staphylococcus albus*, *B. coli*, &c., isolated from the blood-stream, until he adopted a complete non-touch technique for taking blood cultures from the internal jugular vein. The incidence of contaminants was subsequently nil.

He also warned against any attempt to link up any agonal or post-mortem blood cultures positive for *B. coli* with the aetiology of gastro-enteritis, since it is well known that such terminal invasion of the blood-stream by intestinal organisms takes place in many other conditions.

Dr. R. E. Pleasance: *Intravenous anæsthesia in the tropics.*—At the Base Hospital, where I was stationed in India, for a period of two and a half years, intravenous anæsthesia was extensively used. Out of a total of nearly 8,000 anæsthetics, no fewer than 4,000 were intravenous anæsthesias, in some form or other.

In the early stages 91% were given intravenous anæsthesia without combination with any other form of anæsthetic agent. Later, however, this figure was reduced to 40% owing to the need for additional anæsthesia for the more difficult case.

In June 1942 only 24.8% of all cases were given intravenous anæsthesia, but this figure steadily increased, as supplies improved, until in the six months ending December 31, 1944, no fewer than 64.75% of all cases were so anæsthetized.

Preparation of the solution.—Whenever possible the solution was prepared at least twenty minutes before it was required for injection. For ordinary routine short cases a 5% solution was used. This was prepared in the usual manner, 20 c.c. of distilled water being added to the ampoule containing 1 gramme of pentothal sodium. Cases requiring prolonged anæsthesia, except for the initial injection for induction purposes, a 2½% solution.

Cases were divided into those requiring a short anæsthesia and those requiring a long anæsthesia.

The first group were anæsthetized without premedication, as a result of which unconsciousness was not unduly prolonged, and the reflexes were depressed for a short period only, a very important factor where the nursing staff is not too plentiful.

The second group were premedicated with morphine ¼ grain and atropine 1/100 grain, or 1/150 grain for preference, or occasionally with scopolamine 1/100 grain, at least 1½ hours before operation.

Technique of administration.—Four main principles were maintained: (1) That the case was suitable for this type of anæsthesia. (2) That the injection was given slowly and intermittently. (3) Oxygen in adequate supply, and provision for a free airway was at hand. (4) Provision was made for relieving respiratory or cardiac failure.

Five types of cases were dealt with: (1) The simple routine case of short duration. (2) General surgery requiring prolonged anæsthesia. (3) Plastic surgery. (4) Neurosurgery. (5) Thoracic surgery.

Results.—In 4,000 cases there were no deaths, either immediately or remotely connected with this form of anæsthesia. Complications were rare.

Three cases only of venous thrombosis were observed. One after the injection of a 5% solution. A second injection at a later date had no ill-effects. A second case was after the injection of a 2½% solution, and the area where the thrombosis occurred was remote from the site of the injection. The third occurred in a dental surgeon, who had to have a simple whitlow opened. The amount of pentothal used was small, and the operation of short duration.

One case of headache, lasting twelve hours, was recorded.

A number of patients suffering from malaria required operation. These all reacted normally, except that they were found to require less pentothal than the usual patient.

Several developed high temperatures immediately after operation under pentothal. An examination of the blood disclosed the presence of the malarial parasite. All did well and were not adversely affected by the intravenous anæsthesia.

Numerous patients who were having large doses of sulphanilamides were also given intravenous anæsthesia without any subsequent trouble developing.

Several patients with a history of asthma were given pentothal. One for the removal of a foreign body from the lung gave a long history of attacks. In no case was any ill-effect observed.

One case appears of sufficient interest to record.

A soldier, who had been thrown out of an Army truck, pitched on his head, and was brought into hospital unconscious. Colour deeply cyanosed. The only respiratory movement to be observed was that of the diaphragm. At the request of the surgeon "a spot of pentothal" was given to reduce a severe compression fracture of his cervical vertebra. I gave slowly 6 c.c. of a 2½% pentothal solution. The movement of his diaphragm immediately ceased. After the usual period it began to move again, and the operation of reduction was performed.

Comments.—In the tropics, where liver deficiency is likely to occur, due to the various causes so readily obtainable in such a climate, the anæsthetist must be constantly on his guard against the administration of an overdose of pentothal sodium. Especially is this the case with the Indian who requires 30% to 40% less pentothal, as a general rule, than the European.

At the same time the British Other Rank in the tropics requires about 20% less pentothal for a given operation than his fellow in this country.

Atropine should be avoided as a premedicant. Omnopon and scopolamine, or, if not available, morphia and hyoscine, were widely used for this purpose. In addition to being sedative, it was felt that these drugs were less likely to cause disturbance of the heat-regulating mechanism, and thus to diminish another possible factor in the cause of ether-convulsions. As an additional precautionary measure against the occurrence of hyperpyrexia during anaesthesia and operation, mackintosh sheets should not be used to cover the patient. The part played by the skin in regulating body temperature is supremely important in hot climates.

Local and spinal anaesthesia were both used. Hot and dusty climates make it even more necessary to ensure the strictest personal attention to the sterilization of syringes and needles and the use of a rigorous aseptic technique of administration.

Pentothal was, of course, by far the commonest anaesthetic agent used by the Army in the Far East—particularly for battle casualties.

The effect of high altitudes on the administration of anaesthesia.—The barometric pressure at 6,000 feet is 600 mm.Hg or a reduction of slightly more than 20% compared with the pressure at sea-level, and it does have a practical bearing on the administration of gaseous anaesthetics at high altitudes for it means that the pressure of oxygen or of any inspired gas is reduced by the same percentage unless it is administered under pressure. Unless pressure is used it is extremely difficult to produce and maintain anaesthesia with nitrous oxide and oxygen.

Additional oxygen should be given freely with any form of anaesthesia which impairs the normal defence mechanism of hyperpnœa in response to anoxia at high altitudes. The necessity to supply oxygen is not confined only to the administration of inhalational anaesthetics and it should be an invariable accompaniment of intravenous and high spinal anaesthesia in such conditions. The blood picture of people who live for any length of time at high altitudes undergoes a change which affects the administration of anaesthetics.

The patient.—In hot climates the most important thing is to ensure that the sick patient is adequately hydrated. A healthy adult in the tropics loses between 1 and 1½ gallons of fluid per day, even when sedentary. The greater proportion of this is lost from the skin. If the metabolism is raised by fever this loss is greatly increased, and the wise anaesthetist will ensure that the fluid intake of the patient for the twelve hours previous to operation is accurately measured. In cases in which oral intake of fluid is contra-indicated, the pre-operative installation of an intravenous drip is an absolute necessity. Brigadier H. L. Marriott (1945, *Lancet* (i), 679) has stressed elsewhere the necessity also to ensure that the patient has an adequate amount of salt, and he has shown that most forms of heat exhaustion are due to an insufficiency of salt. For this reason, all fluid intake during the twelve hours previous to operation should be salted. A teaspoonful of salt dissolved in 2 pints of lemonade is almost undetectable.

Tropical diseases in relation to anaesthesia.—Malaria is still by far the commonest tropical disease and one with which the anaesthetist is particularly concerned owing to the liability of an injury to precipitate an acute attack of the disease in an already malarious subject. Cases were recorded in which malaria began at the time of operation and the patient had a rigor and presented a clinical picture of malaria during his recovery from anaesthesia. In the difficult days of campaigning on the Burma border in 1942, in one Mobile Surgical Unit, the coincidence of malaria with anaesthesia and operation was so great that quinine, 6½ grains, were added to the pre-operative drip as a routine. There is, however, another undesirable complication of malaria, namely that it engenders in the patient extreme susceptibility to small doses of pentothal. Amoebic dysentery is the other common tropical disease which complicates anaesthesia. In addition to the anaemia, here again there is a liability to impairment of liver function with the consequent need for caution in the exhibition of intravenous barbiturates.

Racial difference.—My personal experience of anaesthetizing natives was extremely limited but the general conclusion with regard to the majority of Indians was that they are more susceptible to intravenous barbiturates and that their blood-pressures tended to be lower than those of Europeans. It was reported that West African natives were sometimes excited rather than sedated by omnopon and scopolamine.

Psychological.—The induction of basal narcosis by means of pentothal is of enormous psychological value among uneducated natives. The fear of mutilation when unconscious is based on religious beliefs and is often a very potent factor if attempts are made to induce anaesthesia by inhalational methods in a conscious patient. This results in determined resistance and prolonged struggling, with their accompanying anxieties for the anaesthetist.

hepatitis. In each case the amount of barbiturate used intravenously must be kept at a minimum.

Indian patients.—(1) The Indian is usually under weight and therefore takes less anæsthetic than the European. This also applies to the amount of sedative necessary for premedication.

(ii) The blood-count is usually low so that adequate oxygen must be given to him. It should be remembered that for major operations a lower pre-operative Hb. may be regarded as more normal than in the European. My old friend and colleague, the late Colonel S. N. Hayes, who had an extensive experience in performing hysterectomies in the Punjab, did not give his patients a pre-operative blood transfusion unless their Hb. was below 35%.

(iii) The Indian usually has a low blood-pressure so that it is reasonable to regard a systolic blood-pressure of 90 mm.Hg as one high enough to proceed to operation instead of 100 mm.Hg as in the European.

(iv) He is more prone to lie motionless and listless after operation than the European, so that it is more essential to make him adhere to the "hourly stir-up" in order to prevent post-anæsthetic chest complications.

(v) The Indian has short air passages, for a tube that has been correctly measured, i.e. twice the distance from the pinna of the ear to the nares, if passed through the nose would, in many cases, enter the right bronchus. Therefore a correspondingly shorter tube is needed for the Indian both for nasal and oral intubation.

(vi) He is an unsuitable patient for local or spinal analgesia unless extremely carefully premedicated. I make this statement in spite of the frequency of spinals and locals in Indian operating theatres—but frequently in that country the operating theatre is not a happy place. Due to the scarcity of trained anæsthetists these methods are safer than the use of inhalation methods, usually chloroform, by the inexpert. The uneducated Indian, like the uneducated throughout the world, is unable to differentiate between touch, pressure and pain. This fact was demonstrated strikingly when I had an opportunity of doing caudals for a number of Cæsarian sections for Indian women. Often the patient would be quite silent until the cry of the infant was heard, then she would shriek violently, for she had realized that she had had a baby and ought to shriek with pain!

Naturally most of my remarks do not apply to those who live completely European lives, for just as we have our problems—the bookmaker and the brewer's drayman for instance—so has India its non-teetotal Sikh!

Dr. Bernard R. M. Johnson: *Anæsthetics in tropical climates.*—The condition of "Heat Hyperpyrexia" is so insidious in its onset and of such a lethal character that it demands the special attention of the anæsthetist practising in the tropics. When it occurs, treatment must be urgent and drastic. All other considerations, either surgical or anti-malarial, must take second place, or the patient will rapidly be lost. The only real remedy lies in prevention, and this can only be attained by training of the nursing staff. They should, in my opinion, be taught to expect the condition to arise in every post-operative case and should live in constant fear of it. European standards of post-operative treatment, with regard to protection from cold, are not easily abolished in the routine of well-trained nursing staffs. Patients should lie post-operatively, wearing only a thin linen cover over the lower part of the body, and a rectal temperature should be taken half-hourly. A steadily rising temperature should demand immediate treatment, i.e. cold sponging, fanning, &c. This record of the body temperature must be charted, and not left to memory and should be continued until consciousness is fully recovered.

Large parts of the tropics, even in peacetime, have very uncertain and unreliable communications—this being so, all outlying districts should be in possession of an Oxford Vaporizer, since supplies of nitrous oxide, cyclopropane, &c., may easily fail, and owing to the humidity of the atmosphere, it is impossible, or almost impossible, to administer open ether.

It was found, not only in Nigeria but in the climate of North Africa and Southern Italy, that it was not necessary to put any water in the water jacket of the Oxford Vaporizer and that, on hot days, it was apparent that a higher percentage of ether was being delivered by the machine than the indicator would lead one to suppose.

More caution than usual should be taken when using the barbiturates in cases of chronic malaria, or in those who have recently suffered from hepatic diseases, when associated with prolonged suppuration. This opinion is based on purely clinical observations as, unfortunately, proper scientific investigation was, for many reasons, not possible.

Dr. Victor Goldman: *Anæsthesia in the tropics.*—The important considerations in discussing anæsthetics in tropical climates may be grouped under the following five headings: (1) Agents and apparatus. (2) Premedication. (3) Fluid loss. (4) Hill stations. (5) Patients—(a) European, (b) Indian.

(1) *Agents and apparatus.*—In tropical climates unless the theatre is air-conditioned, inhalation anæsthetics are rendered difficult on account of rapid vaporization. It used to be said that tough individuals could not be taken to a deep plane of anæsthesia by means of open ether and for that reason chloroform used to be the routine anæsthetic. However, if care is taken ether may be used with success. Ether containers, which should be tins rather than bottles, should be kept in a refrigerator or an ice-chest before opening and the container when in use wrapped up in a damp towel so that evaporation will help to prevent the ether from boiling. A gamgee pad is used on the face and the usual mask with about 12 layers of gauze. This mask is then covered by a second gamgee pad which should not have a hole in it. Ether is dropped on to the outer surface of the top gamgee pad, which is then turned over, and further ether added as required—after each addition of ether the gamgee pad is turned over. Actually induction is rapid in a hot theatre as ether vaporizes so rapidly.

Some experts prefer an inhaler such as a Clover or a Hewitt, but I do not like them unless the bag is dispensed with, owing to the tendency to high concentrations of carbon dioxide that may result. The Oxford Vaporizer is by far the best apparatus for giving ether in the tropics, but if the temperature of the theatre is over 85° F., ice cold water must be placed in the vaporizer instead of hot water.

Ether may be added to gas and oxygen mixtures from a Boyle or similar apparatus without difficulty, and if a closed circuit is employed the canister should be kept in a cool place between cases. To and fro canisters placed near the mask may become overheated. If this happens the canister should be changed or the method discontinued, though an ice-bag wrapped round it will often prevent this eventuality. Chloroform, if used, should be *undiluted with ether*, as mixtures never vaporize in constant percentages.

(2) *Premedication.*—Atropine prevents the normal mechanism of heat regulation by disturbing the action of the sweat glands; for this reason it should never be given to patients before operation in hot theatres. Hyoscine produces the same drying of the secretions of the respiratory tract without the same upset of the heat-regulating mechanism. The combination of morphia and hyoscine was the usual premedication for adults and in children we soon found that small doses of hyoscine were much better than the routine atropine.

If the theatre is air-conditioned the temperature should not be too low, in fact the optimum temperature was found to be 80° F. An important point is that if the patient is not residing in an air-conditioned ward, he should be brought down to the theatre suite at least half an hour before the commencement of the anæsthetic so that his heat-regulating mechanism can become readjusted before he is rendered unconscious.

(3) *Fluid loss.*—Dehydration must be prevented at all costs as fluid loss is considerable for, following the administration of premedication, the patient is not able to drink copiously until he has completely recovered from the anæsthetic. For this reason all patients undergoing an operation which will last for an hour or more should be given an infusion of intravenous saline, and at least a pint an hour can be safely administered. In this connexion it should be stressed that the habit of covering any part of the patient's body with waterproof sheeting must be absolutely prohibited in the tropics.

(4) *Hill stations.*—By the term Hill Stations I mean those that are over 5,000 ft. above sea level, and above those heights it is known that the partial pressure of oxygen in the air is appreciably lowered so that on first arrival in such a station one finds difficulty in walking fast or in climbing hills. After about five or six days there is a physiological increase in the blood-count and effort produces less embarrassment. It was quite common in Murrec, which is 7,000 ft. above sea-level, to get normal counts of 6½ million red cells after a week at that height. For this reason only urgent cases should be anesthetized in such stations unless they have had time to become acclimatized. Even in the acclimatized patient under deep anæsthesia it will be necessary to give additional oxygen under open ether or if the Oxford Vaporizer is employed. This precaution is always necessary during continuous pentothal anæsthetics and high spinals at such altitudes.

(5) *European patients.*—The European tends to take more liquid refreshment in the tropics and is therefore more resistant. He must be allowed to take his usual ration both before and after the anæsthetic. We must always be prepared for the patient who has recently had a course of anti-malarial treatment or who has had an attack of

American anæsthesiologists, but one has gained the impression that they have not fully appreciated its full field of usage nor its importance to the patient.

J. Halton first used d-tubocurarine chloride in November 1944 in an attempt to overcome the disadvantages of the barbiturates consequent on their use as the sole agent to produce anæsthesia in thoracic operations, but it was not until April of last year with the advent of regular supplies that we began to realize its great possibilities. Intocostin was tried, but it seemed to be unreliable in potency, perhaps due to the instability of the solution, and no definite results could be forecast with the samples that we employed. As a result, we returned to the crystalline extract, d-tubocurarine chloride, prepared by Burroughs Wellcome & Co. This has proved of constant potency and very satisfactory.

Pharmacology.—Pharmacologically, the exact nature of the drug is wrapped in much the same mystery as the preparation of the crude poison. The crude extracts are obtained from various vines and plants, and the very nomenclature used to describe these extracts is an indication of our ignorance. Thus that variety delivered to the importers in gourds has been known as "Calabash" or "Gourd" curare, that delivered in earthenware pots as "Pot" curare, and that in bamboo tubes "Tube" curare. This latter is a brown or black shiny resinoid mass, and it is from this variety that the crystalline extract "d-Tubocurarine Chloride" is obtained. Table I shows the alkaloids that have been isolated from the crude extracts.

TABLE I

Tube curare	—————→	Tubocurarine	—————→	Tubocurarine chloride ($C_{25}H_{41}O_4N_2Cl \cdot 2H_2O$)	
	—————→		—————→	Curine ($C_{24}H_{35}O_4N_2$)	Weaker in action. Toxic to heart.
Calabash curare	—————→		—————→	Curarine ($C_{18}H_{24}O_4N_2$)	Extremely potent. Similar effects to tubocurarine. Related to strychnine.
	—————→		—————→	Protocurine ($C_{20}H_{23}O_3N$)	
Pot curare	—————→		—————→	Protocuridine ($C_{24}H_{33}O_4N_2$)	
	—————→		—————→	Protocurarine ($C_{18}H_{23}O_3N$)	Only one giving curare action.

Physiology.—Curare has no action when taken by mouth, hence the perfect safety of the native when he ate his victim after a day's hunting. This immunity is due to detoxication by the liver and not to destruction by the digestive juices. It must be injected either subcutaneously or intravenously. Subcutaneously administered, its action appears in about twenty minutes, but intravenously the action commences within ten seconds, and takes three to four minutes to reach a maximum.

Having entered the circulation it is in part changed by the liver and in part excreted via the kidneys unchanged (Boehm, 1920). It may be noted, in passing, that in the presence of renal damage of any consequence an otherwise safe dose may well cause considerable embarrassment.

It is necessary for a moment to consider the action of curare on (a) the neuromuscular mechanism, and (b) the nervous system.

(a) Claude Bernard (1840), in his classical experiments on frogs, showed that curare produced paralysis of voluntary muscle by an interference with the nerve impulse at the neuromuscular junction. In the curarinized animal both the nerve and muscle are still capable of responding to stimuli, but the break occurs at the junction of the two.

The work of Dale, Feldburg and Vogt (1936), and Brown (1937) and others, leads us to believe that on stimulation of a nerve to voluntary muscle, acetylcholine is produced at the neuromuscular junction, and that curare produces its paralyzing effect by preventing the action of this on the receptor substance of the muscle.

While on this subject it is useful to consider the action of physostigmine which is said to be the natural and physiological antidote to curare.

Normally, acetylcholine is neutralized by an enzyme, cholinesterase, present in the tissues. Physostigmine prevents this neutralization, and so allows an abnormal and excessive barrage of acetylcholine to play on the receptor substance; this may succeed in overcoming its inhibition by curare.

In this series physostigmine has been used on two occasions, and we were not impressed by its action. However, many workers have reported dramatic results, and this is a substance that should always be at hand when and wherever curare is being used.

Mention must also be made of the effect of the climate on the anaesthetist and his assistants. After prolonged exposure to high temperatures and high humidity, even the best men showed a loss of interest and keenness in their work and a tendency to general lethargy.

Major R. P. Harbord asked what was the evidence for the statement that atropine disturbs the heat regulating mechanism more than hyoscine?

Cases coming to operation in the forward areas with malaria were uncommon during the campaigns about the Mediterranean.

Pentothal had been a useful anaesthetic for maxillo-facial surgery in some cases for it shortened the period before intubation and minimized aspiration.

Dr. V. Goldman, in reply to Major Harbord, said that although atropine and hyoscine are close chemical relatives, they produce some different effects when administered. The effects of atropine tend to be excitant, those of hyoscine depressant. Apart therefore from their similar drying effect on mucous membranes, atropine is an opponent of anaesthesia, whereas hyoscine is an adjuvant. Adriani states that the temperature regulating centre is stimulated by large doses of atropine¹; and it is well known that atropine increases the basal metabolic rate.

Dr. G. S. W. Organe asked Dr. Pleasance whether in view of the extremely low incidence of thrombosis he had found after pentothal all patients had been examined with this possibility in view or whether these were merely the cases in which symptoms had presented.

Dr. R. E. Pleasance replied that, as far as was possible, all patients had been examined with this possibility in view.

¹Adriani, John (1942) *Pharmacology of Anaesthetic Drugs*, Second Edition, p. 54. Springfield.

[March 1, 1946]

A Milestone in Anaesthesia?

(d-Tubocurarine Chloride)

By T. CECIL GRAY, M.B., Ch.B., D.A., and JOHN HALTON, M.B., Ch.B.

History.—Curare, the South American arrow poison, has been known since Hakluyt published his account of Sir Walter Raleigh's voyage up the Amazon in 1595.

The exact origin of this "flying death" is still veiled in mystery. Its actual preparation is surrounded by all the esoteric magic and superstition of these strange people descended from the Aztecs, and very little more is known about it now than was discovered by Charles Waterton, a traveller of Lancashire origin, in his journey to the wilds of Demerara in 1812—a journey undertaken with the special object of investigating the origin and preparation of the Wourali poison.

This explorer wrote a book "Wanderings in South America" in 1812, and the description therein of the distillation of the arrow poison from the vine Wourali, the addition of sundry noxious substances, including Indian pepper and the pounded fangs of the Labarri snake, is well worth reading. He tells most vividly of the effects of the poison on various animals. In 1840, Claude Bernard confirmed the observations of Waterton, and attributed the effects of the poison to paralysis due to interruption of the neuromuscular conducting mechanism.

In 1935, Harold King gave the name d-tubocurarine to an alkaloid isolated from tube curare, but little was known until in 1938 Richard Gill (1940), who lived for many years among the Amazons and in the jungles of Ecuador, brought to the United States samples of raw material and of the various plants used in its preparation, and Professor McIntyre (1943) of the University of Nebraska, together with the firm of manufacturing chemists "Squibbs," prepared an extract of standard potency which they labelled "Intocostarin".

In this country, curare was first used by Cole in 1934, Mitchell in 1935, and Ranyard West in 1936, all of whom used it in the treatment of tetanus.

In 1940, Bennett, of Nebraska, described the prevention of trauma during convulsive therapy by the intravenous injection of intocostarin.

In January 1942 Griffith (1944) first used the drug as an aid to anaesthesia in the Homœopathic Hospital of Montreal. It is interesting to note that up to April 1945 Griffith (1945) had only used intocostarin in 300 cases. Since then there has been a flux of articles from

In clinical dosage, little or no effect can be observed on the blood-pressure. Depression may be observed when a large dose of curare is injected quickly, especially if in association with a barbiturate (fig. 2).

Conversely, a slight rise has been occasionally noted (fig. 3), a fact that may be accounted for by the quixotic action of curare on the autonomic nervous system, or in some cases by inadequate ventilation of the lungs with consequent accumulation of carbon dioxide.

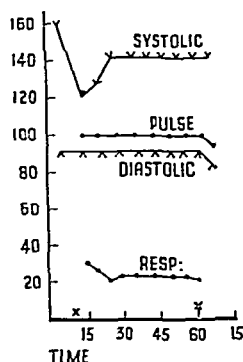


FIG. 2.—Blood-pressure, pulse and respiration in male patient aged 49, undergoing cholecystectomy, with continuous pentothal and curare anæsthesia. (Note initial depression of systolic pressure.)

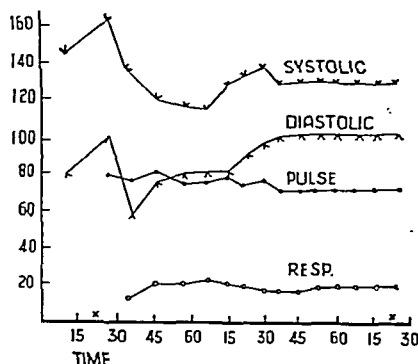


FIG. 3.—Blood-pressure, pulse and respiration in a male patient aged 48, undergoing a partial gastrectomy under pentothal and curare anæsthesia. (Note (i) initial rise in blood-pressure, and (ii) perfect stabilization during the last hour.)

The amazing effect of the arrow poison when injected into an animal has been most beautifully described by Waterton and is worthy of quotation:

"Having procured a healthy full-grown fowl, a short piece of poisoned blow-pipe arrow was broken off and run up into its thigh, as near as possible betwixt the skin and the flesh, in order that it might not be incommoded by the wound. For the first minute it walked about, but walked very slowly, and did not appear the least agitated. During the second minute it stood still, and began to peck the ground; and ere half another had elapsed it frequently opened and shut its mouth. The tail had now dropped and the wings almost touched the ground. By the termination of the third minute it had sat down, scarce able to support its head, which nodded, and then recovered itself, and then nodded again, lower and lower every time, like that of a weary traveller slumbering in an erect position, the eyes alternately open and shut. The fourth minute brought on convulsions, and life and the fifth terminated together."

In the conscious human subject the muscles of the eyes, mouth and fingers are affected first, then those of the trunk and limbs, and finally the diaphragm. Consciousness is retained, and recovery occurs in the reverse order, being complete in about thirty minutes from a single injection. American workers (Whitacre and Fisher, 1945) have actually pushed the drug beyond the stage of diaphragmatic paralysis, and obtained unconsciousness. This seems to us a completely unjustifiable procedure, and the narcosis may well have been due to anoxia, although curare may have some action on the synapses of the central nervous system, in view of the fact that there is some evidence that here too acetylcholine plays some part in impulse transmission.

Technique.—The tubocurarine when first received must be sterilized. It has been our custom to autoclave the dry powder at 10 lb. pressure for thirty minutes, and cultures taken from the solution have proved sterile. Moisture must not be allowed to enter the phial during autoclaving as the powder becomes discoloured and presumably unfit for use.

After the usual premedication, in our cases morphia 1/6 grain and atropine 1/150 grain to 1/100 grain, anæsthesia is induced with whatever may be the agent of choice.

The curare, not itself an anæsthetic, is used as an adjuvant in order to obtain good relaxation at any time and in a very light plane. It is injected as and when required, allowing the requisite three to four minutes for it to take effect.

Three main techniques have been employed:

(1) The single dose method, for the induction of anæsthesia, short operations and endoscopies, oral and anal.

Employed in this way a mixture of 15 mg. of tubocurarine with 0.5 gramme of pentothal is injected fairly rapidly. After two or three minutes respiration becomes very shallow or ceases altogether, the jaw is completely relaxed and there is no spasm or cough when an airway is inserted or an endotracheal tube is passed. Furthermore, the

That, briefly, is how curare produces its relaxation, which makes it of such great value to the anaesthetist.

(b) *The effect of curare on the nervous system.*—Acetylcholine appears to perform some function in the transmission of nerve impulses through the ganglia of the autonomic system, and possibly also through all the synapses of the central nervous system. In the same way that curare prevents the acetylcholine-receptor substance union at the neuromuscular junction, so too does it in the autonomic nervous system.

Although this is said to be only a secondary effect of curare, exerted perhaps only in the presence of large doses, yet it may well be of importance clinically.

In the first place, curare appears to depress markedly the laryngeal and bronchial reflexes, preventing that troublesome complication and bane of the anaesthetist, spasm. Secondly, the effect on the gut has been of some interest. Solis-Cohen (1928) states categorically that curare causes contraction of the gut, and Griffith (1945), the pioneer, has stated that in cyclopropane-curare anaesthesia the gut is indeed contracted, but Cullen (Gross and Cullen, 1945) has produced experimental evidence in animals that it is flaccid and inactive. We have noted marked contraction and activity in most cases, but in others, including most of those anaesthetized with barbiturate-curare only, this irritability has been absent. It is difficult to come to any conclusion in this matter, as the gut reaction will vary with the premedication and the anaesthetic agents. All the anaesthetic and narcotic drugs, not to mention atropine, act on the autonomic ganglia, and it may well be that we are observing a summation of these effects in conjunction with curare.

A clinical difficulty arises in cases of ulcer perforation when we believe that this very real activity of the gut may be responsible for flooding the peritoneal cavity with stomach contents. Furthermore, in a case undergoing transplantation of the right ureter under cyclopropane curare anaesthesia, the ureter had to be inserted into the ascending colon, as the descending part was so contracted that it was impossible to mobilize it. This excessive contraction is never seen when the barbiturates are used to produce anaesthesia.

Present pharmacological opinion is that the liver and kidneys are completely unaffected by curare, but its action on the heart and cardiovascular system is a matter of some importance. The information available up to now has been of doubtful value, for one has never been quite certain which particular extract or preparation was being used. Certain extracts of curare, curine in particular, are known to be potent cardiac poisons. As it seemed that tubocurarine was a definite and specific substance it was clearly of value to investigate its cardiac effects further. Moreover, our clinical results led us to believe that the drug might have some effect on the myocardium.

This work is still in progress, but one of us (T. C. G.) has observed the effect of tubocurarine on the electrocardiogram in a number of cases in the human subject, and with the assistance of Dr. Gregory, of the Department of Physiology in the University of Liverpool, has estimated the result when this material is injected into the Starling heart-lung preparation in dogs. The investigation has progressed sufficiently for us to say that d-tubocurarine produces no effect on the electrocardiogram in the doses in which it is used clinically (fig. 1), and on injection into the heart-lung preparation in dogs, using a dosage vastly greater than anything ever likely to be used in humans, no effect whatever has been observed on the cardiac rate output, or on the venous pressure. As the output is maintained and the venous pressure unaltered, it can justifiably be assumed that there is no alteration in the coronary flow.

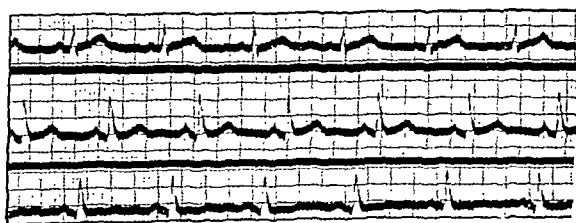


FIG. 1.—Electrocardiogram taken seven minutes after the administration of 0.5 grammes pentothal and 20 mg. curare.

It must be emphasized that, in spite of this, curare must be used only with the greatest possible care to maintain full and very complete oxygenation, otherwise the patient's condition will rapidly deteriorate. Especially is this so in those cases having a poor myocardium, for they cannot cope with any sub-oxygenation after curare.

We had employed curare in only a few cases when it became obvious that some form of synergism existed between the drug and the barbiturates, and a further synergism between this combination and any inhalational agent which might be used, such as ether or cyclopropane.

Four facts led us to this conclusion:

(1) From experience we know the dose of barbiturate required to prevent "movement response" to painful stimuli (incision of the skin) in the average patient. For convenience let us call this the minimal anæsthetic dose (M.A.D.).

(2) Curare is not an anæsthetic, and in small doses does not prevent movement. 17.5 mg. were given to a conscious patient. He was still able to react by movement to a noxious stimulus.

(3) The administration of the combination of 15 mg. of curare and a dose of barbiturate less than the M.A.D. produces a completely anæsthetic and motionless patient.

(4) If any inhalational anæsthetic is used to supplement this barbiturate-curare combination, only a minimal amount is required to produce deep anæsthesia.

Signs of anæsthesia and curarinization.—One of our first observations was that here one is deprived of all the ordinary classical signs for estimating the depth of anæsthesia. The eye reflexes, corneal and conjunctival, owing to paralysis, are absent or sluggish, and the ordinary respiratory signs are modified, for at any rate in upper abdominal operations sufficient curare must be given to paralyse the intercostals. The three criteria which do remain are the pulse, respiratory rate, and the anæsthetist's experience.

Frequent observation of the pulse is essential; the first sign of inadequate anæsthesia is a rising pulse-rate and failure to notice this may result in the onset of severe shock due to inadequate narcosis. An increase in respiratory rate will also give warning, provided the patient is not apnœic.

The anæsthetist's experience is often the best guide as to the amount of any particular anæsthetic required to keep a patient in a light plane, and the necessity for the would-be user of curare to have this experience cannot be over-emphasized. At the same time, the danger of a paralysed patient waking up and becoming all too conscious of what Sassoon describes as "the dull opiate throb which was his wound" is non-existent, for in the dosage in which it is used, as already stated, curare does not prevent the small movements of a limb which indicate returning consciousness. An observation was made by Ranyard West (1936) that some specimens of curare had a "lissive" action, producing relaxation without actual paralysis. With tubocurarine a perfectly relaxed abdominal musculature may be present in a patient who is still able to respond to painful stimuli by movements of a limb.

There are two signs of curarinization which must be mentioned. The first is the typical respiration characterized by a pushing-out of the lower part of the chest and of the abdomen with each diaphragmatic contraction, and accompanied by a jaw and tracheal tug. This is not the same as the gasping respiration seen in deep ether anæsthesia, when a partially paralysed respiratory centre is endeavouring to cope with the situation. It is at this point that all effort should be concentrated on ensuring full ventilation of the lungs. Should this not be maintained, the condition will deteriorate, and the surgeon will be embarrassed by the exaggerated diaphragmatic excursion. In this event control of the respiration with the rebreathing bag is easily attained.

The second sign, and a most valuable one, is the ease with which the lungs may be inflated by pressure on the rebreathing bag (Morton, 1945). The absolute intercostal and abdominal relaxation, with the complete absence of laryngeal spasm, makes this manœuvre easy and satisfying.

Recovery.—Any therapeutic innovation must be judged first on the dangers involved in its exhibition to the patient, and secondly on the results obtained.

In respect of the dangers involved in the use of this drug they are real, but so are they throughout the whole realm of anæsthesia. It can be stated that in the hands of the competent anæsthetist, fully conversant with the treatment of the apnœic patient, and with the dosage and technique already described, far from being a danger it will prove an incomparable boon.

Regarding the second criterion, the results of the administration of tubocurarine may be regarded from the point of view first of the surgeon and secondly of the patient.

patient is able to tolerate straight away, without distress, an anæsthetic vapour strong enough to maintain the anæsthesia should this be desired. Induction time is thus tremendously shortened.

With this dose bronchoscopy is easily performed, and because of the relaxation of the pharyngeal and anal sphincters, œsophagoscopy or sigmoidoscopy can be carried out with ease.

Patients recover quickly after this form of administration.

(2) For longer procedures in conjunction with the intermittent injection of an intravenous barbiturate. A remote control tap has been devised which facilitates this technique. Its use overcomes two difficulties of administration, namely, the arm can be placed in any position during the operation without fear of the intravenous needle becoming displaced, and precipitation of the barbiturate by the curare is prevented. This is of little importance where pentothal is concerned, since the precipitation is reversible, but it is of major importance if kemithal or other barbiturate is used. The essential details of this apparatus were shown later to the Meeting in a film.

After an induction as described above, small increments of barbiturate and curare are made. 0.1 gramme of pentothal and 2 to 4 mg. of curare are given from time to time as the reaction of the patient to stimuli and the demands of the surgeon dictate. If the length of the operation is such that a dose of more than 1.5 grammes of pentothal or 3 to 4 grammes of kemithal has to be exceeded, which occurs very rarely, we prefer to continue the anæsthesia with minimal amounts of cyclopropane or ether.

(3) As an adjuvant to inhalational anæsthesia. The intermittent fractional injection of a total dose of 15 to 30 mg. of curare is utilized to produce relaxation while still keeping the patient in a light plane of anæsthesia.

Whichever of these three methods is used, oxygen must be supplied in abundance, and preferably by means of a closed circuit, for by this means adequate and complete ventilation of the lungs can be ensured. The importance of this artificial ventilation of the lungs in cases of overdosage must have been known to the Indians of old, for our respected friend Waterton (1812) mentions that: "It is supposed by some that wind introduced into the lungs by a small pair of bellows would revive the poisoned patient, provided that the operation be continued for a sufficient length of time." In order to confirm this, this enterprising traveller performed the following experiment:

"A she-ass received the Wourali poison in the shoulder, and died apparently in ten minutes. An incision was then made in its windpipe, and through it the lungs were regularly inflated for two hours with a pair of bellows. Suspended animation returned. The ass held up her head and looked around, but the inflating being discontinued she sank once more in apparent death. The artificial breathing was immediately recommenced, and continued for two hours more. This saved the ass from final dissolution; she rose up and walked about; she seemed neither in agitation nor in pain."

Was this, written about the year 1812, the first description of controlled respiration, a technique the knowledge and practice of which is common and essential in modern anæsthesia?

Dosage.—The margin between effective and over-dosage is small. In our opinion no exact dosage for weight scale can be worked out, but the very obese require a little more than average and the extremes of age considerably less. Further, it must be remembered that in computing dosage 1 mg. of d-tubocurarine chloride is approximately equivalent to 6.6 units or milligrams of intocostarin. 20 mg. is sufficient to relax the average healthy adult's abdomen; and 25 mg. to paralyse the diaphragm. The effect of this initial dose will last for a varying time up to forty minutes. There is some temporary cumulative effect, so that subsequent doses must be considerably less, and it has been found satisfactory to use 2 to 4 mg. increments for maintenance. We have never had to use a total dosage of more than 45 mg. of tubocurarine, even when prolonged diaphragmatic paralysis was desirable.

Both extremes of age are very susceptible to curare, and small doses only must be used. In the aged—and the drug has been used in patients over 80—an initial dose of 10 mg. is suitable. Children up to 12 years should not be given more than 6 mg. for induction.

It has been stated that when ether is being used the dose of curare should be reduced by one-third, ether itself being said to have a curariform action. This, in our opinion, is a wrong approach to a correct clinical observation.

mitted, but ordinarily would have been tolerated, probably terminated life. It is our opinion that anoxia and not curare was responsible for these fatalities.

The assessment of results following thoracic operations is difficult. Comparative figures are hard to obtain, anæsthetic methods have been constantly changing, and with the advent of curare more extensive surgery has been successfully practised on cases of the poorer risk type, a fact which speaks for itself!

Table III shows the incidence of post-operative pulmonary morbidity in patients undergoing operations in the upper abdomen. These are compared in column 3 against the figures given by three observers, King (1933) and Campbell and Gordon (1942) using various types of anæsthesia for similar operations. It is necessary to point out that it has been considered a post-operative complication if a patient develops a cough with any physical signs, or suffers aggravation of an existing chest disease.

TABLE III.

Operation	No. of cases	Pre-op. chest condition		Post-op. chest condition	Comparative figures
		Minor	Major		
Partial gastrectomy	38	26.3%	—	18.4% }	38.3% }
Gastro-enterostomy	22	27.3%	—	12.7% }	(King, 1933)
Cholecystectomy	43	16.0%	2.3%	7.0% }	24.1% }
					(King, 1933)
Upper laparotomy	15	20.0%	13.3%	6.7%	
Other upper abdom. operations...	7	—	14.3%	14.3%	
Total percentages		22.5%	3.2%	12.5%	56.5% (Campbell and Gordon, 1942)
Total number of cases	125	27	4	15	

We have for long subscribed to the view that heavy premedication with opiates is a thing to be deprecated. The result of this, even before the introduction of curare, was the occasional occurrence of restlessness post-operatively, especially when the main anæsthetic agent was one of the barbiturates. The restlessness which has occurred in a small proportion of these cases has, we are sure, been due to following this principle. Coupled with this, the patients are so well that they are able to exhibit a well-marked second stage "coming up," as it were. They are very conscious of any noxious stimuli, such as wound pain, splintage, or inflated catheters.

This unease has only been transient, and does not occur since we adopted the rule of giving as a routine 1/6 grain morphine and 50 mg. pethidine prior to leaving the theatre.

Indications for use.—Every thoracic and abdominal case undergoing a major operation is benefited by the exhibition of curare. The thoracic case benefits from curare in several ways. It is our considered opinion that for this type of surgery the barbiturates are probably the best agents, always provided that the dosage can be kept at a minimum. By their use the inhalation of irritating vapour is avoided, respiration is quiet and, since they are rapidly eliminated, post-operative toxic sequelæ do not appear, and recovery is rapid and uneventful. The addition of curare to this form of anæsthetic technique considerably reduces the amount of the barbiturate required. Cough and spasm are eliminated and control of diaphragmatic movement can be achieved rapidly and at will, yet the full cough reflex is present before the patient leaves the table.

Curare is of very special benefit to the poor-risk patient. The bad chronic chest case who must undergo a major operation even in the upper abdomen is a subject who will owe a lot to the arrow poison.

In peripheral circulatory failure we see a state of affairs that really does call for its use.

In deep anæsthesia the vasomotor central control is disturbed. This has been demonstrated by Zweifach and co-workers (1945) in a series of experiments on animals, in which they observed the power of adjustment of the capillaries of the mesentery to graduated bleedings under various anæsthetics. Under all deep anæsthesia with the possible exception of cyclopropane, the vasomotor compensatory reaction was lost so that the animal did not respond to transfusion as it should. This may not occur under light anæsthesia, and a glance at the pressure curves of patients undergoing abdomino-perineal operations, a procedure likely to cause a degree of shock and involving a change of position, shows striking clinical confirmation of this.

It will be seen that in fig. 4, where the anæsthetic was cyclopropane and ether carried to a deep plane, the blood-pressure falls progressively when the patient is put into the lithotomy position. This phenomenon has been observed constantly and the chart

To the surgeon the results must be satisfactory, for he is presented with "blotting-paper" relaxation at any time and quickly, together with a quiet operating field.

In respect of the patient, many factors must be considered. Dr. Ralph Waters (1944) made a most important observation when he said that the relief of pain has always exacted a price, due in some part to the toxicity of the drugs used, but more often through ineptitude in the care of the patient when under their influence. This price is paid in the operating theatre, and afterwards in the ward. For one pneumonia caused by ether vapour, many more are caused by mechanical obstruction of the airway during the operation or in bed when the patient is lying motionless on his back recovering from the anæsthetic, possibly inhaling vomitus or septic oral secretions.

Again, vomiting with varying degrees of liver and kidney damage may be caused in some part by the anæsthetic agent exhibited, but more often by long periods of anoxia attendant on its use.

How does the method we have described compare with these dicta? First consider the drugs. Curare is completely and very rapidly eliminated. There is no evidence that it has any latent toxicity. The same holds good for the barbiturates in the doses in which they are used. If inhalational anæsthesia is employed to supplement, the amount is so small that the risk of toxic after-effects is non-existent or greatly reduced. During the anæsthesia the patient is ventilated by an atmosphere rich in oxygen and since spasm of the cords is completely eliminated the chance of anoxæmia arising is extremely remote. Vomiting in thoracic cases is now a thing of the past. In abdominal cases, while the incidence appears unchanged, the degree of severity is very much less.

It is on return to the wards that the biggest price is so often exacted. But in these patients the essential reflexes are fully recovered prior to leaving the theatre, and within half an hour they are co-operative, able to do breathing exercises, to cough and expand their chests, and can be left with safety to look after themselves. This has meant a tremendous reduction in post-operative pulmonary morbidity.

Between us we have given curare to 1,049 cases, and Table II shows the extent of the ground we have covered.

TABLE II.

<i>Thoracic operations.</i>						
Pneumonectomies	15
Lobectomies	38
Thoracotomies	73
For stricture of the œsophagus	2
Cervical sympathectomy	1
Thoracoplasties	211
Subphrenic abscess	1
Minors	183
						524
<i>Abdominal operations.</i>						
Gastrectomies	38
Other gastrics	22
Cholecystectomies	43
Upper laparotomies	15
Lower laparotomies	25
Splenectomies	2
Œsophageal myotomies	2
Hydatid cyst of liver	1
Excision of rectum	12
Entero-anastomoses	6
Hemicolectomies	15
Appendicectomies	12
Lumbar sympathectomies	2
Pre-sacral neurectomies	1
Gynæcological	14
Genito-urinary	25
Epigastric herniæ	2
Incisional herniæ	8
Inguinal herniorrhaphies	8
Minors	22
						269
<i>Head and neck operations.</i>						
Thyroidectomies	5
Other major	3
Laryngeal intubations only	35
						43
<i>Orthopaedic operations.</i>						
Major	47
Minor	106
						213
Total						1,049

Two deaths which might be attributed to the anæsthetic have occurred. They happened early in the series. The post-mortem findings in each case showed gross myocardial damage, and that, coupled with a degree of anoxia which should never have been per-

Professor Charles A. Wells mentioned that much of the work had been done in, and with the co-operation of, the Department of Surgery for which he was newly responsible in Liverpool.

Every advance demanded its own sacrifice, but in this instance there had been no human sacrifice. To the contrary, he was satisfied that many patients were alive and well to-day who would not have survived other anaesthetics and, further, that satisfactory operative relief had been made available, through curare, to many patients to whom it would otherwise have been denied.

The surgeon was given a quiet field with full relaxation without apparent prejudice to the general condition of the patient. If the anaesthesia was becoming light, warning was often given by phonation or the movement of a limb. Abdominal straining was a late feature of the waking process and a deeper plane could be recovered in a few seconds, before any embarrassment was experienced.

On returning to the wards, the patients not only wakened quickly but were unusually co-operative and were able to begin, almost at once, the limb movements and breathing exercises which were so vital to quick recovery and low morbidity.

Dr. F. Prescott described some experiments that he had made in collaboration with Dr. Organe. In the unanaesthetized subject it was found that 10 mg. of d-tubocurarine chloride intravenously had very little effect in relaxing voluntary muscle. Only the muscles of the face and eyes were affected to any extent. A dose of 20 mg., however, produced paresis of the muscles of the face, neck, arms, legs and abdomen in that order. Speech was lost but not the cough reflex. Respiration was not consciously affected, but spirometer readings showed that the tidal air was diminished by about one-third. A dose of 30 mg. intravenously produced complete paresis of all voluntary muscle and almost complete cessation of respiration, necessitating artificial respiration to prevent asphyxia. No analgesic action was observed. A test was made to see if fractional administration gave relaxation without respiratory suppression. A dose of 30 mg. given intravenously at the rate of 1 mg. per minute did not produce adequate relaxation. The subject was not curarized and was able to sit up ten minutes after the injection. A curarizing dose in the conscious patient lasts for twenty to thirty minutes. A more prolonged effect without depression of respiration was produced by giving 15 mg. intravenously and 15 mg. simultaneously by the intramuscular route.

Dr. F. Barnett Mallinson said he was surprised at the condemnation of intocostin. He had been using this preparation of curare since the end of 1944 and he had been very satisfied with the results. Using intocostin only he found himself very much in agreement with the speakers' experience of curare, and would add that he had never had to use prostigmin.

He had never used the Burroughs Wellcome preparation, first, because intocostin has worked so well; second, because shortly after he published his preliminary report on curare in anaesthesia (*Lancet*, July 21, 1945) he had had two reprints and a personal communication from Dr. Ranyard West (*Journ. Physiol.*, 1938, p. 437; *Lancet*, February 19, 1938, p. 432) whose work had already been quoted by Dr. Gray, warning him of the dangers of bronchospasm. This he had never encountered with intocostin. He would like to ask the speakers whether they had encountered this complication. Also did they consider that the Burroughs Wellcome preparation would become available in solution, like intocostin?

Liberal oxygen should always be a feature of the accompanying anaesthesia, and he suggested that cyclopropane was thus the best. On the other hand, 2.29 grammes pentothal (a pretty big dose) with N_2O-O_2 for a normal length gastrectomy seemed likely to have been sufficient in itself and hardly to have needed the addition of curare.

A true evaluation of the real safety of curare must await cases in their tens of thousands. Chloroform was widely considered to be the most dangerous of all anaesthetics; but taking into account its accepted mortality rate, it might require some 4,000 administrations before the anaesthetist had a death. He doubted if the total published administrations of curare yet reached 4,000.

Dr. T. A. B. Harris noted, in the series of cases described, that d-tubocurarine had been used in 126 genito-urinary cases. Since, as far as is known, curarine is excreted from the body solely by the kidneys, would Drs. Gray and Halton consider renal inefficiency to be a contra-indication to the use of curarine?

Dr. C. Langton Hewer queried the method of sterilizing curarine chloride. He doubted whether autoclaving the ampoule did in fact sterilize the contained powder.

Dr. Hewer also described several cases of ocular paresis which had occurred after curare had been used. In a series of 37 administrations (mostly for gastrectomy) 19% of patients complained afterwards of difficulty in fully opening their eyes or of blurred vision. In every case symptoms had disappeared by the fourth day. Dr. Hewer pointed out that in myasthenia gravis, a condition very similar to curarization, the patients often complained first of the same symptoms.

Dr. G. S. W. Organe stressed the importance of adequate ventilation as well as adequate oxygenation. In one experiment on a conscious subject the tidal volume was reduced to less than 100 c.c. Although, breathing pure oxygen, there was no cyanosis, there was considerable distress and a feeling of suffocation due, probably, to accumulation of carbon dioxide. The dose was extremely critical. After 10 mg. tubocurarine intravenously on the same subject, the minute volume was 12 litres; after 20 mg. it fell to $7\frac{1}{2}$ litres and after 30 mg.

shown is typical of twenty such. Fig. 5 is illustrative of six similar cases anaesthetized in a light plane with the help of curare. No fall in blood-pressure occurs on the change of position. We attribute this to an intact vasomotor central mechanism, which enables the patient to adapt his circulation to the altered circumstances.

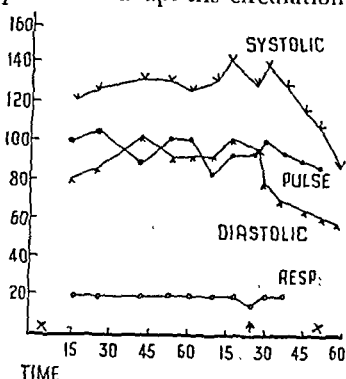


FIG. 4.—Blood-pressure, pulse and respiration in a male patient aged 41, undergoing abdomino-perineal excision of the rectum. Anaesthesia: Hexobarbitone induction, cyclopropane and ether maintenance. (Note the blood-pressure falls when the patient assumes the lithotomy position as indicated by the arrow.)

Contra-indications.—Curare should never be used by anyone who is not fully conversant with the care of the apnoeic patient. Anoxia appears easily and is more serious, especially when there is cardiac inefficiency. Despite laboratory evidence that the drug has no cardiac action, clinically there is no doubt that with this form of anaesthesia patients do not tolerate even a slight degree of anoxaemia.

In abdominal operations when used with cyclopropane it may cause excessive contraction of the gut, and so render surgery more difficult.

Curare should not be used in cases of intestinal obstruction with distension, unless particular care is taken to avoid the uncontrolled regurgitation of the intestinal contents in these patients whose every natural protection has been removed. This also applies to cases with a lung abscess.

The dosage may have to be modified in the presence of renal damage of any consequence.

West has described the occurrence of excessive bronchial secretion and spasm in some of the cases he treated for tetanus. In our series of cases, including many oral endoscopies, this has never been observed.

Finally, this drug should not be used in cases suffering from myasthenia gravis.

CONCLUSION

The road lies open before us, and with a grave and insistent warning to the inexperienced that we are dealing with one of the most potent poisons known, we venture to say that we have passed yet another milestone, and the distance to our goal is considerably shortened.

We express our deep gratitude to Professor Charles Wells, Mr. H. Morriston-Davies, Dr. Minnitt, Mr. J. A. Martinez, and our friends and colleagues, the surgeons, who have made this work possible.

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Section of Surgery

President—ERNEST FINCH, M.D., M.S., F.R.C.S.

[February 6, 1946]

DISCUSSION ON CARCINOMA OF LOWER ŒSOPHAGUS AND CARDIA

Mr. Norman C. Tanner: Carcinoma of the œsophagus, usually a squamous-celled tumour, and carcinoma of the cardia, usually an adenocarcinoma originating in gastric mucosa, differ in their histology, direction and rate of spread, prognosis and treatment, but the technical problems associated with their extirpation are similar.

The surgical inaccessibility of the œsophagus was one of the chief technical barriers to its extirpation and many ingenious approaches to it have been described and used. The poor suturing qualities of the œsophagus and the apparent impossibility of restoring intrathoracic continuity gave rise to every conceivable variety of antethoracic œsophagoplasty being tried. Now, as a result of improvements in thoracic surgery, in anaesthesia and in chemotherapy, a more merciful and more direct approach to these cases has arisen, making resection and immediate restoration of continuity a possibility in nearly all the early œsophageal and upper gastric neoplasms.

The abdominal approach.—A purely abdominal resection, or total gastrectomy, is a suitable operation where the upper limits of a gastric tumour just encroach on the lower limits of the cardia. We are considering, however, the tumour which starts in the region of the cardia and has œsophageal as well as gastric extension. While a palliative excision of the hopeless case may be justifiable by a purely abdominal approach, if curative surgery is aimed at, the abdominal approach will be found insufficient in such cases, for the tumour mass gets in the way of œsophageal anastomosis. The œsophagus seems to be shortened and made rigid by growth and one will generally find, if the cardia is really involved, that the transection is through or lamentably near the edge of the growth.

1940-1945 ADENOCARCINOMAS INVOLVING CARDIA—38				1940-1945 SQUAMOUS-CELL CARCINOMA OF LOWER ŒSOPHAGUS—14			
No operation	2	No operation	2
Laparotomy, inoperable, nil done	4	Gastrostomy only	5
" " Gastrostomy	5	Thoracotomy, inoperable, nil done	1
" " Palliative œsophagoplasty	6	Thoracic resection and antethoracic œsophagoplasty	4
" " or short circuit	13	Intrathoracic resection and anastomosis (plus 1	2
" " Palliative total gastrectomy	3	simple ulcer)
Collo-abdominal resection	3				
Thoracic or abdomino-thoracic resection	5				

I have never performed œsophagectomy without some attempt at immediate reconstruction of the œsophagus. Earlier on I erroneously formed the opinion that where possible thoracotomy should be avoided and antethoracic anastomosis favoured in the poor risk case. Therefore I will first describe my experiences with extrathoracic anastomosis.

Extrathoracic anastomosis.—Three resectable adenocarcinomas of the cardia were treated on similar lines. In each case a mid-epigastric incision was made, and the part of the stomach involved mobilized. Next the œsophageal hiatus was enlarged by an anterior incision in the diaphragm, exposing the base of the pericardium. Into the opening the whole hand could be placed behind the heart, and the lower œsophagus freed under vision. The middle œsophagus was freed blindly and another incision in the left suprasternal notch enabled the upper œsophagus to be mobilized, the hand in the posterior mediastinum doing most of the work. Under vision the œsophagus was divided well above the growth and the cardia and affected part of the stomach and glands removed, the rest of the œsophagus being pulled out of the neck. It was then pulled under the skin of the chest wall.

The first case so treated was a man aged 73. The pyloric antrum only was preserved, as the growth involved half the stomach, and the pyloric antrum was pulled under the skin of the chest wall and anastomosed to the cut end of the œsophagus. The intention was to enable the patient to feed for a few days and when the œsophagus sloughed to do a dermatoplasty after the method of Rovsing. Post-operatively a left tension pneumothorax was treated by needling and pulmonary œdema on the second day was treated by postural drainage. After that he ate and drank and seemed well. On the eleventh day the œsophagus was exposed and the sloughing part removed. A rubber tube was stitched into the pyloric antrum. Unfortunately the latter was an awkward shape and leaked badly, so that it was difficult to feed him. Eventually he went downhill and died at the end of a month.

to only 2 litres. In curare we had not found the answer to all post-operative complications—in one man with perforated gastric ulcer there developed a post-operative lobar collapse. The general condition of patients after major upper abdominal operations was as good as when muscular relaxation had been obtained with intercostal nerve block and the procedure involved was much simpler and quicker. Tracheal intubation was not called for in such cases as it was particularly easy to maintain a clear airway. He had not seen bronchospasm and had used curarine chloride to relieve laryngospasm.

Dr. A. H. Galley, in answer to a query raised by Dr. Geoffrey Organe over an experiment he had performed on a conscious colleague by injecting tubocurarine chloride, said that the respiratory distress suffered by the subject of Dr. Organe's experiment was due to an accumulation of carbon dioxide in the blood-stream in excess of the normal. If one was subjected to simple and uncomplicated oxygen lack, unconsciousness would ensue without any feeling of distress; but, if one held one's breath, or the air passages were blocked, or ventilation became so shallow as to interfere with respiratory exchange, then carbon dioxide—having little or no means of escape—would accumulate with subsequent distress. Although this feeling would not be experienced by the unconscious patient, Dr. Organe's experiment did remind them that such shallow breathing would inevitably lead to carbon dioxide accumulation with the well-recognized cycle of events which led to circulatory collapse. It might be better, therefore, always to employ closed circuit machines when administering oxygen to curarized patients.

Dr. H. W. Loftus Dale had also observed that operations such as cholecystectomy, gastrectomy, and abdomino-perineal excision of rectum could be performed under light cyclopropane anaesthesia and curare with no, or insignificant, alterations in pulse and blood-pressure.

Since curare produces no sensory loss, and only light planes of general anaesthesia were employed, there seemed nothing to prevent "nociceptive" afferent stimuli from reaching the vasomotor centre. Unless this could be explained by synergism between curare and the general anaesthetic agent, as suggested by the openers, doubts must be cast on the theories of Crile and others concerning "reflex shock". A practical point: In one case in which an endotracheal tube packed off with gauze was used to protect the tracheo-bronchial tree against aspiration, a seal tested and found gas-tight became totally inadequate after the injection of curare owing to relaxation of the pharyngeal muscles, and a considerable amount of extra packing was required to ensure against leakage.

Dr. J. W. Trevan said that there was little doubt that the active principle of intocostrin was d-tubocurarine. This was claimed by the makers, and the speaker had examined the alkaloid separated by Dr. Copp from a sample of intocostrin, which accounted for the activity of the extract and which as far as tests could be carried out on the small sample proved to be d-tubocurarine. He found that 1 unit of a sample of intocostrin he had examined was equal in activity to 0.17 mg. of d-tubocurarine. He said that confusion had arisen by labelling doses in terms of milligrammes of a preparation of curare. d-Tubocurarine apparently differed from crystalline curarine from *strychnos* species in having a strong curarizing activity without other marked toxic properties. d-Tubocurarine was derived from *chondrodendron tomentosum*. Prostigmine and physostigmine were true antagonists to d-tubocurarine, in a dose about 1/20 to 1/10 of the dose of d-tubocurarine. Very large overdoses (3 to 4 times paralyzing dose) were not, however, antagonized by prostigmine or physostigmine. He saw the experiment on Dr. Prescott and could not agree that the prostigmine injected did not accelerate his recovery. The antagonism of tubocurarine by prostigmine on isolated voluntary muscle was quite certain.

The Openers, in reply, expressed their interest in Dr. Prescott's observations; clinically they were of great value. Answering Dr. Mallinson they reiterated their remarks on the inconsistent action of intocostrin. d-Tubocurarine chloride, on the other hand, was a specific alkaloid and produced a constant and predictable action in the human subject and on experimental animals. The gastrectomy which required 2.29 grammes of pentothal lasted two hours yet the patient was able to answer questions before leaving the theatre; his recovery was uneventful. Was Dr. Mallinson able to produce that result with pentothal alone?

Comparison between chloroform and tubocurarine was not logical, for while the former was a proved somatic poison, all clinical and laboratory evidence showed that this was not so with the latter drug. In reply to Dr. Harris, gross renal damage, proved or suspected, was a contra-indication to full doses of tubocurarine.

In reply to Dr. Langton Hewer, no case of ocular paresis had been seen in the series under discussion. With regard to sterilization, it was admitted that the method at present in use was open to criticism and it was under review. Nevertheless, samples of the solutions taken at random had always proved sterile.

All the points made by Dr. Organe were of great importance. They could not be stressed enough especially to those anaesthetists who were about to use tubocurarine for the first time.

Dr. Trevan's observations were noted with interest and further clinical investigations would obviously have to be made.

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Gastrostomy only	5
Thoracotomy, inoperable, nil done	1
Thoracic resection and antethoracic œsophagoplasty	4
Intrathoracic resection and anastomosis (plus 1 simple ulcer)	2

I have never performed œsophagectomy without some attempt at immediate reconstruction of the œsophagus. Earlier on I erroneously formed the opinion that where possible thoracotomy should be avoided and antethoracic anastomosis favoured in the poor risk case. Therefore I will first describe my experiences with extrathoracic anastomosis.

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The first case so treated was a man aged 73. The pyloric antrum only was preserved, as the growth involved half the stomach, and the pyloric antrum was pulled under the skin of the chest wall and anastomosed to the cut end of the œsophagus. The intention was to enable the patient to feed for a few days and when the œsophagus sloughed to do a dermatoplasty after the method of Rovsing. Post-operatively a left tension pneumothorax was treated by needling and pulmonary œdema on the second day was treated by postural drainage. After that he ate and drank and seemed well. On the eleventh day the œsophagus was exposed and the sloughing part removed. A rubber tube was stitched into the pyloric antrum. Unfortunately the latter was an awkward shape and leaked badly, so that it was difficult to feed him. Eventually he went downhill and died at the end of a month.

The second was a man aged 71, with a carcinoma of the cardia and 2 cm. of the œsophagus. Less stomach had to be resected here and so a tube of greater curve of the stomach, after the method of Rutkowski, was made. This time much less œsophagus was retained, and sutured to the tube of greater curvature. The patient stood the operation well, but the anastomosis began to leak in five days and was resutured. He died on the fifteenth day from cellulitis of the chest wall.

The third case was a very atheromatous man of 66. The stomach was severely involved in the growth as well as œsophagus, and a total gastrectomy and splenectomy had to be done. This time the jejunum was widely mobilized after the method of Roux and Yudin and the œsophagus anastomosed to jejunum. Again it was obvious that the œsophagus would slough, for in view of the atheroma it was only possible to bring the jejunum up to mid-sternal level. Therefore the lower œsophagus and anastomosis were left above the skin level with the intention of enclosing it in skin shortly after. The patient withstood the operation well and was taking diet well on the day after operation. On the second post-operative day, the skin of the chest wall was mobilized to form a skin tube round the exposed œsophagus. He died on the fourth post-operative day of pulmonary œdema.

Four cases of antethoracic œsophagoplasty performed after resection of squamous-celled tumours of the lower œsophagus were briefly: exposure of the growth by right or left thoracotomy, removal, and then pulling the upper œsophageal stump out of an incision in the left suprasternal notch. After closing the chest the abdomen was opened and the stomach completely mobilized, and drawn out of the abdomen and then brought under the skin of the chest wall to meet the œsophagus. This type of anastomosis has been successful in a case of Hermon Taylor's and was originally suggested by Kirschner for innocent stricture of the œsophagus.

In the first case, a man of 63, I made the mistake of not resecting the tumour before pulling the upper œsophageal stump out of the neck, and so he developed a post-operative mediastinal emphysema and died within twenty-four hours. In this case an attempt to make the œsophageal ends meet failed and so the cardia was left as a gastrostomy opening.

In the second case, a man of 68, the cardia was removed with the growth and a satisfactory anastomosis was made between the œsophagus and fundus of stomach. This patient died on the third post-operative day, autopsy showing severe pulmonary œdema and purulent bronchitis.

The third case, a man aged 50, had a very extensive growth, both pleural cavities being opened, and he died of pulmonary œdema on the second day.

The fourth case, a fragile and wasted woman of 64, had a similar procedure and did well at first. However, the suture line leaked on the eleventh day and was resutured. This recurred on the nineteenth day. At the end of a month a local dermatoplasty was done. She eventually died at the end of nine weeks of exhaustion from repeated leaks.

These cases demonstrated that while they are radical and the aged patient in most cases easily withstood the surgical shock, he could not withstand the exhaustion following repeated leaks from the subcutaneous anastomosis.

Intrathoracic anastomosis.—The eight cases of intrathoracic reconstruction were as follows:

Adenocarcinoma of the cardia:

The first was admitted in December 1943. A laparotomy was done, and carcinoma involving the upper quarter of the stomach and coronary glands was found with a small metastasis in the liver. In view of his comparative youth (48) the operation was continued: the stomach being freed and divided below the growth. Next the left chest was opened, the diaphragm opened and after resection of the lower third of the œsophagus and upper quarter of stomach, an œsophago-gastric anastomosis was made. He made a good recovery interrupted by a mild pleural infection. He went back to work for several months but died of metastases eleven months later.

The next, a man of 65, with congenital choreo-athetosis, was found to have a neoplasm fairly localized to the cardia and lower œsophagus. His growth was exposed by removal of the 8th left rib and parts of the 5th, 6th and 7th, and after division of the diaphragm the growth was mobilized. The lower half of the œsophagus, cardiac end of stomach and spleen were removed, and œsophagus united to gastric stump. He made an excellent recovery and still swallows well nine months after the operation. However, the growth was extensive, with metastases in three lymph glands, and he has now developed a small umbilical metastasis.

The third case was a man aged 72, with a similar tumour. A similar left major thoracotomy exposed the growth. Unfortunately, the tumour was found to be infiltrating the œsophageal hiatus in the diaphragm and so an extensive operation was necessary, with removal of the upper quarter of stomach and glands, lower third of œsophagus, spleen and ring of diaphragm. Post-operative purulent bronchitis and pulmonary œdema were treated by postural drainage. He improved, but suddenly died on the eleventh day, from pulmonary embolus.

The fourth case, an obese man of 65, had a similar tumour of the cardia, but there was also a large hiatal hernia, and it appeared that the growth had originated in, or had caused, a short œsophagus. A similar operation was performed but he developed pneumonia and died on the fifth day.

The fifth case was interesting in that there was very extensive gastric and œsophageal growth in a patient aged 68 necessitating total gastrectomy and splenectomy. The upper jejunum was divided and mobilized after the method of Roux and Yudin, and the proximal

end implanted lower down in the jejunum. The jejunum was passed through the transverse mesocolon and the abdomen closed. The left chest was then opened and the œsophagus further mobilized, and then the stomach, spleen and lower œsophagus were pulled out of the chest and removed. An anastomosis was made between the œsophageal stump and the jejunal end, and the chest closed with drainage (fig. 1). He made an excellent recovery and before discharge was able to take a three course meal with a glass of stout, was keen on his meals and found brandy gave him a pleasant epigastric glow!



FIG. 1.—X-ray of barium swallow following intra-thoracic anastomosis of cut end of œsophagus to end of mobilized jejunum.

Squamous-celled œsophageal carcinomas:

The first was an atheromatous and somewhat bronchitic man of 75, who had a squamous-celled carcinoma at the junction of the middle and lower œsophagus proved by œsophagoscopy. The tumour was approached by a left-sided thoracotomy. He had an advanced tumour adherent to the lung margin and with enlarged glands. A most fortunate circumstance was that he had such an extreme degree of tortuosity of the aorta resulting from atheroma that the growth had lost any relationship to the aorta, making removal easier. The growth was removed, together with glands, adjacent pleura and a small fragment of lung tissue. The stomach was mobilized, brought through the diaphragm and anastomosed to the œsophageal stump. This patient made an excellent recovery, interrupted by a short period of cardiac insufficiency, but was up, about and eating well at the time of his discharge. I believe this patient is the oldest to have survived this type of operation (75)—a fact which is of importance in a disease which is especially one of old age.

The next patient, a female aged 67, with paralysis agitans, was diagnosed radiologically as carcinoma of the lower œsophagus: operation was on the same lines as the last patient and she made an excellent recovery and was discharged well. Section, however, showed the stenosis to be due to scarring of a peptic ulcer, but I have included it as it presents a similar technical problem.

The last carcinoma of the lower œsophagus in this series was just above the junction of the middle and lower thirds, and I already felt with these in this position that there was some difficulty in making a section really well above the tumour, if the anastomosis was to be made under the aortic arch. One could, of course, transfer the upper stump above the arch, and make a high anastomosis lateral to the aorta, but then one finds that, at the beginning of the operation, one is working in difficulty in the lower part of the wound, and the rest of the operation one is working in difficulty in the highest part of the wound. Now in June 1945 I had a patient with a high carcinoma of the œsophagus in whom I first opened the abdomen and freed the stomach along both curvatures, leaving the right gastric and right gastro-epiploic arches intact. Next I widely opened the diaphragm by cutting forwards from the œsophageal hiatus to expose the base of the pericardium and then largely under vision mobilized the lower quarter of the œsophagus.

Next I opened the right chest high up by excising the 5th rib. The growth was inoperable but it was a simple matter by traction on the œsophagus to pull the stomach into the right chest and make a short circuit between fundus and higher œsophagus.

I decided to use a similar method on this patient, a rather alcoholic man aged 69, whose growth was at 35 cm. from the incisors. The stomach and lowest œsophagus were freed abdominally, and the diaphragm opened. Next I performed a right thoracotomy removing the 6th rib and the azygos vein was tied and divided. The growth was very widely removed, and the stomach easily pulled up and its fundus anastomosed to the œsophageal stump (fig. 2). X-ray shows a high anastomosis. This patient made an excellent recovery interrupted by a transfusion jaundice, but was discharged eating and feeling well.



FIG. 2.—X-ray of barium swallow showing very high intrathoracic anastomosis and stomach shadow above level of clavicles.

Mr. Ivor Lewis described a similar but two-staged method in a recent Hunterian Lecture and had a success by it before my first case. However, to one who does not claim to be primarily a thoracic surgeon I think mobilization of the lower œsophagus and division of the diaphragm through the abdomen is easier than the ingenious trans-thoracic method favoured by Mr. Lewis, and it seems that the patients will tolerate a one-stage procedure.

Resection of the Cardia and Lower Œsophagus

(1) *Antethoracic anastomoses*.—7 cases, average age 65: 3 survived two to nine weeks. None left hospital.

(2) *Intrathoracic anastomoses*.—8 cases, average age 66: 6 left hospital well.

(3) *Abdominal resections*.—Mostly palliative—13.

As regards feeding these patients pre-operatively none had a gastrostomy or jejunostomy, but all were given as much fluid protein by mouth as they could take, and in addition had intravenous plasma and saline daily.

The anaesthesia in each case was a posterior intercostal block on the side of the thoracotomy, and abdominal field block on the other side if the abdomen was to be opened, and each was given cyclopropane through an intratracheal tube with an inflatable cuff, by Dr. P. Peterson.

No patient had either a temporary or permanent interruption of the phrenic nerve.

Post-operatively the most troublesome complication was pulmonary œdema, which usually arose about the second day and was often accompanied by cardiac irregularity and bronchitis. The treatment we found most satisfactory was postural drainage and postural coughing, the bed being placed in the Trendelenburg position several times a day.

CONCLUSIONS

It is obvious from my results that I must favour intrathoracic anastomoses.

Finally, I would like to point out several advantages which one may gain from a preliminary laparotomy, except in the very localized and very low œsophageal tumour.

(1) Greater ease in freeing the stomach and a better dissection of the subdiaphragmatic and coronary lymph glands, and of the lesser omentum.

(2) Greater facility in mobilizing the jejunum in the rare cases where a loop of jejunum is too short to reach the œsophagus.

(3) Greater ease in closing the duodenum in cases where the whole stomach has to be removed.

(4) The ability, after dividing the diaphragm from below, to insert the hand in the posterior mediastinum and to palpate the growth, and possibly avoid a fruitless thoracotomy. In one case by this means I was able to ascertain with certainty that an œsophageal neoplasm was invading the bifurcation of the trachea.

(5) The ability to make a higher resection and anastomosis very comfortably by combining abdominal mobilization of the stomach and lower œsophagus with a high right thoracotomy.

Mr. P. R. Allison: Carcinoma involving the cardia may be of gastric or œsophageal origin, and it is often impossible to distinguish these on clinical and radiological evidence only. From the point of view of surgical treatment they are one problem, though differences in extent of involvement of stomach or œsophagus may need corresponding modifications of procedure. All these growths are hopeless when attacked from the abdomen, but the approach through the left pleural sac, with splitting of the diaphragm, has offered a good hope of palliation and some chance of radical treatment. The work is still young and includes much which might be called experimental so that the figures quoted must not be accepted as indicating all that can be offered to these patients. Progress is being made in technical details from one patient to the next, and many years must elapse before the results of these can be gauged. As in all forms of cancer the urgent call is for earlier diagnosis, and it is one of the purposes of this paper to indicate some of the ways in which this could be achieved.

Out of 100 patients suffering from malignant obstruction in the region of the cardia, 41 were found to have squamous carcinoma, 53 adenocarcinoma, 4 undetermined, 1 reticulum-cell sarcoma, and 1 Hodgkin's sarcoma. Both œsophageal and gastric growths were more common in males than in females, and the ages varied from 30 years to 77 years (Table I).

TABLE I.

	Males	Females	Oldest	Youngest	No. between 30 and 40 yrs.	Average age
Squamous carcinoma 41	29	12	73	30	3	55
Adenocarcinoma 53	35	18	77	31	6	57

DIAGNOSIS

The commonest symptom of which patients complain is dysphagia, and one of the main causes of delay in treatment is the astonishing pertinacity with which they carry on before seeking advice. In this series the average duration of dysphagia after which the patients were first seen was five months and this was the same for the œsophageal as for the gastric growths. The longest time was two and a half years. The longest time-lapses were found in those whose investigation had been incomplete or faulty and whose symptoms had been partially relieved by the passage of bougies or Hurst's mercury tube. This latter instrument, which has been so useful in its day, should now be ejected from our armamentarium, as its place in the treatment of cardiospasm should be taken by Negus' hydrostatic dilator, and its use in other conditions is both illogical and harmful. Dysphagia may sometimes be intermittent due to the sloughing away of masses of growth or to the alternate impaction and dislodgement of unchewed solid food. There is no relation between the length of history or rate of progress of dysphagia on the one hand, and the extent of growth or degree of malignancy on the other. Emphasis should be laid on this point when the question of suitability of a patient for operation is being considered. In one case where the growth attained huge dimensions, there was no history of dysphagia at all but only feul eructations. It is true in the main, however, that a growth starting in the abdominal œsophagus or in the stomach close to the cardia is more likely to give rise to dysphagia as a first symptom than those further away. A carcinoma in the body of the stomach may cause loss of appetite, loss of vigour and anæmia for some time before it reaches the cardia and produces dysphagia.

Pain is variable in its incidence, type and degree. It is often absent altogether even in hopeless cases. Epigastric discomfort or pain behind the lower end of the sternum

Next I opened the right chest high up by excising the 5th rib. The growth was inoperable but it was a simple matter by traction on the œsophagus to pull the stomach into the right chest and make a short circuit between fundus and higher œsophagus.

I decided to use a similar method on this patient, a rather alcoholic man aged 69, whose growth was at 35 cm. from the incisors. The stomach and lowest œsophagus were freed abdominally, and the diaphragm opened. Next I performed a right thoracotomy removing the 6th rib and the azygos vein was tied and divided. The growth was very widely removed, and the stomach easily pulled up and its fundus anastomosed to the œsophageal stump (fig. 2). X-ray shows a high anastomosis. This patient made an excellent recovery interrupted by a transfusion jaundice, but was discharged eating and feeling well.



FIG. 2.—X-ray of barium swallow showing very high intrathoracic anastomosis and stomach shadow above level of clavicles.

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Resection of the Cardia and Lower Œsophagus

(1) *Antethoracic anastomoses*.—7 cases, average age 65: 3 survived two to nine weeks. None left hospital.

(2) *Intrathoracic anastomoses*.—8 cases, average age 66: 6 left hospital well.

(3) *Abdominal resections*.—Mostly palliative—13.

As regards feeding these patients pre-operatively none had a gastrostomy or jejunostomy, but all were given as much fluid protein by mouth as they could take, and in addition had intravenous plasma and saline daily.

The anaesthesia in each case was a posterior intercostal block on the side of the thoracotomy, and abdominal field block on the other side if the abdomen was to be opened, and each was given cyclopropane through an intratracheal tube with an inflatable cuff, by Dr. P. Peterson.

No patient had either a temporary or permanent interruption of the phrenic nerve.

Post-operatively the most troublesome complication was pulmonary œdema, which usually arose about the second day and was often accompanied by cardiac irregularity and bronchitis. The treatment we found most satisfactory was postural drainage and postural coughing, the bed being placed in the Trendelenburg position several times a day.

CONCLUSIONS

It is obvious from my results that I must favour intrathoracic anastomoses.

Finally, I would like to point out several advantages which one may gain from a preliminary laparotomy, except in the very localized and very low œsophageal tumour.

(1) Greater ease in freeing the stomach and a better dissection of the subdiaphragmatic and coronary lymph glands, and of the lesser omentum.

(2) Greater facility in mobilizing the jejunum in the rare cases where a loop of jejunum is too short to reach the œsophagus.

(3) Greater ease in closing the duodenum in cases where the whole stomach has to be removed.

(4) The ability, after dividing the diaphragm from below, to insert the hand in the posterior mediastinum and to palpate the growth, and possibly avoid a fruitless thoracotomy. In one case by this means I was able to ascertain with certainty that an œsophageal neoplasm was invading the bifurcation of the trachea.

(5) The ability to make a higher resection and anastomosis very comfortably by combining abdominal mobilization of the stomach and lower œsophagus with a high right thoracotomy.

Mr. P. R. Allison: Carcinoma involving the cardia may be of gastric or œsophageal origin, and it is often impossible to distinguish these on clinical and radiological evidence only. From the point of view of surgical treatment they are one problem, though differences in extent of involvement of stomach or œsophagus may need corresponding modifications of procedure. All these growths are hopeless when attacked from the abdomen, but the approach through the left pleural sac, with splitting of the diaphragm, has offered a good hope of palliation and some chance of radical treatment. The work is still young and includes much which might be called experimental so that the figures quoted must not be accepted as indicating all that can be offered to these patients. Progress is being made in technical details from one patient to the next, and many years must elapse before the results of these can be gauged. As in all forms of cancer the urgent call is for earlier diagnosis, and it is one of the purposes of this paper to indicate some of the ways in which this could be achieved.

Out of 100 patients suffering from malignant obstruction in the region of the cardia, 41 were found to have squamous carcinoma, 53 adenocarcinoma, 4 undetermined, 1 reticulum-cell sarcoma, and 1 Hodgkin's sarcoma. Both œsophageal and gastric growths were more common in males than in females, and the ages varied from 30 years to 77 years (Table I).

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simple stricture and "cork-screw œsophagus". The ultimate differentiation should depend on œsophagoscopic appearances and, if necessary, biopsy. There seems to be no record yet of a simple peptic ulcer of the œsophagus undergoing malignant change.

A final diagnosis of the cause of dysphagia should not be made in any but the most decrepit without an endoscopic examination. The œsophagus above a malignant stricture may or may not be dilated, but if dilatation is present it is never extreme. Fluid and food retention may be noted, and the mucous membrane shows a corresponding amount of chronic inflammation. This last is most marked just above the stricture but it is hardly ever the angry change which may be seen in the acid digestion of a case of simple peptic ulcer. The site of obstruction may be smooth and funnel-shaped where the growth has extended mainly in and outside the wall, or masses of neoplasm may be seen in the lumen. A careful note should be made of the smell. Sometimes ulceration is associated with a mixed infection which produces a most offensive odour and in these cases the greatest care must be exercised to avoid contamination of the mediastinum at operation. If the growth starts in the stomach and has not invaded the œsophageal mucosa, a hardness or rigidity or deformity may be noted at the lower end. The instrument, which normally passes easily into the stomach, meets an obstruction and the cardia fails to relax. If a bougie is passed gently into the stomach at this stage the stenosis can be appreciated by the hand. A rigidity and fine roughness is transmitted, and felt to be quite unlike the soft grip sometimes experienced in cardiospasm. It may be possible to confirm the diagnosis by biopsy even when the growth itself cannot be seen.

PATHOLOGY

The primary growth, whether it be in the œsophagus or stomach, may extend mainly into the lumen of the organ. In this case a polypoidal mass occurs which may attain large proportions before giving rise to many symptoms. Such tumours are more likely to be found in the œsophagus than in the stomach, for in the latter position peptic digestion with sloughing of the mass usually occurs. The spread within the wall may take place in the submucous, muscular or surrounding tissues. It is not uncommon in the œsophagus to find islands of growth separated from the main mass by normal mucosa. It is important to determine this when the patient is œsophagoscoped so that impalpable growth is not left behind at operation. In some of the cases examined there has been a notable spread of growth within the muscular tissue of both stomach and œsophagus. In one gastric growth nerves were found containing tubular extensions of malignant cells. When the growth extends beyond the œsophagus it invades the mediastinal tissues, pleura and lung. Perforation into the lung with gangrene and a spreading bronchopneumonia is one of the accidents which may cause death in these patients. At the cardia or in the body of the stomach a direct spread may occur either to the left lobe of the liver or the body of the pancreas. Spread to lymphatic glands may occur early or late depending on the type of tumour. An appreciation of the lymphatic paths is essential if a radical operation is to be employed. Those in the stomach have been worked out by Jamieson and Dobson (1907), and it is on their work that the following description is based.

The lymphatics of the upper half of the stomach pass mainly along the left gastric vessels through or past various gland stations to the glands around the celiac axis. Some vessels, particularly from that area where the blood drainage is through the vasa brevia, pass in the gastrosplenic omentum or over the top of the lesser sac of peritoneum into the pancreatico-lenal glands. The greater curvature area drains along the right gastro-epiploic vessels to the subpyloric glands, but this region is only of importance where the growth is so extensive as to need a total gastrectomy. In addition to these three main catchment areas there is a lymphatic pathway from the cardia through the œsophageal hiatus of the diaphragm upwards to the glands in the posterior mediastinum. Vessels may by-pass their immediate gland stations and drain into other glands some distance away and, in the post-mortem room, a specimen has been seen where a growth at the cardia was associated with a lonely metastasis in a gland on the right side of the œsophagus at the level of the vena azygos major where this vessel enters the superior vena cava.

The lymphatics of the lower œsophagus drain mainly into the para-cardiac and superior gastric glands, communicating freely at the cardia with the gastric lymphatics but some pass upwards in the posterior mediastinum to the tracheobronchial groups of glands.

TREATMENT

The treatment of this group of cases has been varied according to the general state of the patient, the local condition of the growth and our own experience.

33 of these patients were so ill or so advanced in disease that no treatment other than simple medical care could be offered to them. The hindrance to active measures was not usually age, but the extent of the growth when first seen, the presence of clinically evident secondary deposits, advanced cardiovascular degeneration and concomitant disease in other organs. Of the 67 patients for whom something was attempted, a Souttar's tube was inserted in 14, and radiotherapy given with or without radon in 7. The low proportion treated by radiotherapy has depended upon a number of factors one of which has been the shortage of plant, staff and bed accommodation during the war years. No deductions can be drawn from these patients other than that temporary relief from

on swallowing may occur in gastric or œsophageal lesions respectively, and the latter may come on after the act of swallowing saliva, without food being taken. It is sometimes difficult to decide when a patient has real pain and when he suffers intense annoyance and inconvenience from the impaction of food in the stricture. Severe pain, especially when it radiates into the back, is of evil significance and usually indicates fixation of the growth. This does not necessarily mean that it is irremovable, for involvement of the pancreas can be overcome by the resection of the body or tail of this organ. Sometimes, however, pain in the back would appear to be caused by fixed malignant glands around the cœliac axis. In 2 patients the first symptom was a soreness of the right side of the neck. It is not possible to do more than guess at the explanation of this. Other symptoms that have been noted are heartburn, belching, sometimes with the bringing up of foul-smelling wind, anorexia, hiccough, hæmatemesis and loss of weight. Loss of weight is purposely put last on the list, not because of its infrequent occurrence, but because the emphasis usually placed on this symptom is a potent cause of late recognition of cancer. Hiccough is a relatively rare symptom but it is interesting to note its occurrence in this series. It was complained of in 6 cases. All of these had squamous growths. It was the first symptom in all 6, and the growth was found on œsophagoscopy at 40 to 41 cm. from the alveolar margin in 4, and at 37 cm. in 2.

Physical examination often fails to further the diagnosis and should reveal nothing in the operable case. A tumour in the epigastrium suggests an advanced lesion, while a gland in the neck or mass in the rectum banishes all hope.

The radiography of lesions at the cardia calls for the greatest care, skill and experience if anything but an advanced growth is to be detected. The careful study of the movements, and the mucosal patterns of the œsophagus and stomach in the upright, prone, supine and Trendelenburg positions is necessary. A review of the X-ray appearances of the present series carried out with Dr. A. S. Johnstone, shows that malignant lesions in the lower œsophagus and upper part of the stomach fall into more or less well-defined groups:

A. *Growths Confined to the Œsophagus.*

In these a small length of normal œsophageal mucosa can usually be demonstrated below the growth. They may be subdivided into:—

- (1) Local ulcer.
- (2) Massive tumour: (a) in the lumen and pedunculated; (b) in the lumen and sessile; (c) centrifugal growth with large soft tissue shadow.
- (3) Intermediate group, with new tissue formation and ulceration keeping pace.
- (4) Extensive superficial ulceration.

B. *Growths Occurring at the Gastro-œsophageal Junction.*

These may be œsophageal or gastric in origin, and it is not possible to tell the one from the other by X-ray examination.

C. *Growths Obviously Arising in the Stomach.*

These may be classified into:

- (1) Those giving a picture very like cardiospasm.
- (2) Those showing a horizontal deformity of the abdominal œsophagus.
- (3) Massive carcinoma of the body of the stomach extending up to the cardia.
- (4) Carcinoma of a herniated gastric fundus.

The local ulcer may be missed unless the mucosal pattern is carefully studied; it is most amenable to surgical removal. The massive tumour is not likely to be overlooked. Its recognition as a separate type is useful inasmuch as it may be easily resected in spite of its forbidding appearance. In the pedunculated variety the lumen is seen to be on one side of the mass whereas in the other two the barium passes down the middle of the tumour. The œsophagus which shows extensive superficial ulceration is of pathological interest because it is not uncommon to find islands of ulcerated neoplasm separated from one another by areas of unaffected or leukoplakic mucous membrane. The growths of the stomach which most often cause difficulty in diagnosis are those at the cardia which infiltrate mainly beneath the mucous membrane, and give rise to a picture very like cardiospasm or produce a horizontal deformity of the abdominal œsophagus. These patients are too often treated either by the physician or the endoscopist by repeated blind or œsophagoscopic dilatation. The development of a gastric cancer in the fundus of the stomach which has herniated into the mediastinum has been noted in 5 cases. This may cause difficulty in diagnosis unless the hernia is carefully sought in the Trendelenburg position.

It is worth noting that no case of a small annular malignant stricture at the lower end of the œsophagus has been observed in this series.

The differential diagnosis is mainly to be made from cardiospasm, peptic ulcer of the œsophagus, which has been found fifty times during this period of study, simple tumour,

TECHNIQUE

Pre-operative.—Where possible a good mixed diet is given. When dysphagia is present a high-calorie fluid diet is prescribed, and solids are avoided in order to prevent obstruction and minimize œsophageal irritation above the growth. In this way the fluid content of the body is restored. The blood-count is brought up to normal by transfusion. During the short period of investigation and preparation smoking is prohibited and breathing exercises given to mobilize the chest. Oral infection has been vigorously treated, but it has not been considered necessary to remove teeth as a routine.

Anæsthesia.—After preliminary morphia and scopolamine, sodium pentothal is given into the blood drip. The œsophagoscope is passed and all fluid aspirated. The lower œsophagus is sprayed with penicillin powder and a "Tampax" pack is left in the œsophagus just below the cricoid. Silk thread attached to this is left hanging out of the mouth. Between 9 and 14 c.c. light nupercaine are injected intrathecally when the patient is in position on the right side. The lungs are kept at the required degree of inflation by oxygen given through a face-piece and pharyngeal tube, and unconsciousness is then maintained by nitrous oxide or sodium pentothal as the situation warrants.

Operation.—The approach now used is through the left pleural space after resection of the whole of the 9th rib and cartilage and the posterior end of the 8th. The left phrenic nerve is crushed and local anæsthetic injected into the mediastinum around the œsophagus. The left dome of the diaphragm is split and the extent of the lesion ascertained. The œsophagus above the growth is first mobilized and a fully curved anastomosis clamp applied so that septic fluid cannot escape up the œsophagus from an infected ulcer during the manipulation of the stomach. An effort is made to free the whole area to be removed before the gut is cut, but this has sometimes been impracticable. The stomach is divided and closed first. A second clamp is then applied to the œsophagus above the first, and this is divided after a swab has been placed in the mediastinum behind it. The anastomosis is made between the lower end of the œsophagus and the anterior surface of the stomach. The stomach is then drawn up in front so that the suture line is sunk in a peritoneal cuff. Catgut seems to be quite suitable for the anastomosis but more emphasis must be placed on accuracy of apposition than on materials used. If omentum is available it is wrapped round the junction. Penicillin powder has been applied to the mediastinum in recent cases. The diaphragm is lightly sutured round the stomach and a few interrupted stitches are used to fix the stomach to the diaphragm. The lungs are inflated at intervals during the operation. They are finally inflated when the wound is closed, and an under-water drain inserted. At the end of the operation the œsophagoscope is passed, the pack removed and any fluid or blood aspirated.

Post-operative treatment.—Breathing exercises and frequent changes of positions are prescribed from the first day. Drinks of water or glucose are given in small quantities as soon as the patient wants them. After forty-eight hours tea, milk and dilute fruit drinks are taken, but always washed down with water. After four days, the patient is back on the high-calorie fluid diet including jellies, junket, &c.

The drainage tube is removed after forty-eight hours, and the patient is allowed out of bed on the sixth or seventh day. Aspiration of the chest is carried out as and when required.

REFERENCE

JAMIESON and DOBSON (1907) *Lancet* (i), 1061.

Mr. Ivor Lewis: In cancer of the œsophagus pre-obstructive symptoms are not uncommon. Unfortunately, however, they seldom worry the patient enough to take him to the doctor, and are in any case not likely to suggest the diagnosis. Several of my œsophagectomies have had such symptoms; ensiform pain during swallowing, a cough, hiccups, soreness between spine and scapula. Only in the last-named, however, did the symptoms result in the true cause being diagnosed before obstruction had supervened. *Dysphagia* thus remains the presenting symptom of carcinoma of the œsophagus. It must always be investigated both by X-rays and œsophagoscopy. I agree with Mr. Allison that all cases of cardiospasm must be œsophagoscoped.

A positive biopsy should be the rule before major thoracotomy. In one mid-œsophagus obstruction I had reason to regret this; on thoracotomy no growth could be felt; the chest was closed. On further reference to the section it was highly suggestive only, and should really have raised a serious doubt before deciding on a major exploration. As for the technical problems, I have no experience of presteral œsophagogastrotomy and am interested to hear that Mr. Tanner has abandoned it. For growths of the lower end the one-stage transpleural, transphrenic operation, through the bed of the left 8th rib, should displace all others. The present practice of œsophageal resection is based on the idea of throwing the thoracic and abdominal cavities into one so as to mobilize some part of the abdominal alimentary canal, to secure anastomosis with the œsophagus without

obstruction has been achieved and that it has often seemed worth while. Some operative procedure was attempted on 49 patients. In 11 of these a thoracotomy or laparotomy was done only to find the condition hopeless. In 4 a jejunostomy was done in preparation for a further attack which never materialized. In the early years an attempt was made to obtain relief from obstruction by making a cervical œsophagostomy and connecting this by a rubber tube to a jejunostomy. This was done for 3 patients and then abandoned. At this time also 1 patient was treated by total gastrectomy by the abdominal route, and survived three months. The remaining 30 patients were subjected to a major transthoracic operation, of which 9 were œsophagectomies or œsophago-gastrectomies with a view to extrathoracic reconstruction, 14 œsophago-gastrectomies with mediastinal anastomosis, 2 resections of the whole stomach and lower œsophagus with mediastinal anastomosis between œsophagus and jejunum, and 5 palliative œsophago-enterostomies without resection of growth.

This means that 75 patients in the series were hopeless from the point of view of excision when first seen. The figure is actually worse than this because, of those resected, some were done with the knowledge that the operation could not be considered anything but palliative. The results of surgery cannot be judged on the number of five-year survivals. Obstruction at the cardia causes such discomfort and distress that its relief, even for a few months, is worth achieving, and when a patient has been subjected to a major operation he is entitled to expect some benefit. Nevertheless the aim should be to perform a radical operation where possible, and it is therefore worth while to consider a basis for this which will stand the test of anatomy and physiology and what is known of the pathology of these tumours. The object is in the first place to remove the primary tumour with its area of lymphatic drainage, and secondly to restore continuity of the digestive tract.

It would appear that a radical operation for a growth at the cardia requires the removal of the lower segment of the œsophagus, the fundus and most of the lesser curvature of the stomach, the gastro-hepatic omentum as close to the liver as possible, the left gastric vessels with associated lymphatic glands right back to the cœliac axis, the body and tail of the pancreas and therefore of necessity the splenic vessels and spleen, and as much cellular tissue around the œsophagus as possible at least as far as and including the gland at the level of the inferior pulmonary vein. This formidable undertaking has been the basis of the attack on these tumours during the last few years, and although discretion has been used in its application to particular cases, it seems that a truly radical operation is no worse tolerated than half-measures, by both surgeon and patient alike. A high mortality is more likely to be caused by technical errors involving soiling of the mediastinum or leakage of the anastomosis, than by the slightly increased time and shock involved in the careful dissection of the lymphatic bed.

In the first 9 patients operated upon the growths were excised with a view to an external plastic operation being performed later. All these patients are dead. 3 died from infection following operation, 1 from uræmia eight weeks after operation, 4 from secondary deposits within twelve months and 1 from cardiac failure four years after excision of the growth. A post-mortem examination was obtained in the case of this last patient, and no secondary deposits were present. A plastic operation by skin tube was completed in only 2 cases, 1 of which was the patient who survived and swallowed through her new œsophagus for four years. She was previously shown to this Society.¹ The other died from secondary deposits after twelve months and at autopsy a typical peptic ulcer was found at the junction of skin tube and stomach.

In 14 patients resection with mediastinal anastomosis was carried out, and in one of these the anastomosis had to be performed above the aortic arch on account of the extension of the growth up the œsophagus. Of these, 6 died as a result of the operation, 1 from a leaking anastomosis, 1 from shock, and in this patient malignant glands had to be left around the aorta, 2 from sepsis in mediastinum and pleura, 1 from a fistula at the anastomosis which developed ten days after operation, and 1, the patient in whom the anastomosis was performed above the aorta, from torsion of the stomach and œsophagus on their long axis, causing complete obstruction of the œsophagus. Of the 8 who survived, 3 have already died with secondary deposits, at intervals of nine months, twelve months and fifteen months. The cause of death in the last patient was chronic nephritis but at autopsy small secondary deposits were found in the liver and para-aortic lymph glands. One of these patients developed a peptic ulcer at the anastomosis which responded to dilatation through the œsophagoscope followed by medical measures. There are, therefore, 5 patients still alive and their operations were one, three, three, seven and twenty-four months ago.

Resection of the whole of the stomach and the lower end of the œsophagus was done in 2 patients but in 1 of these the lesion turned out to be a Hodgkin's sarcoma. Both survived the operation, but the one with a very extensive carcinoma died at home three months later. The other is still alive five months after operation but has a mass in the abdomen for which he is receiving X-ray therapy. In this latter case the anastomosis was performed between the œsophagus and a length of intestine mobilized on an elongated mesentery after the method of Roux and recently revived by Yudin. The ability to mobilize such a loop from a thoracic approach raised the possibility of side-tracking irremovable growths and so relieving obstruction. It was urgently necessary to be able to do this in certain cases of peptic ulcer of the œsophagus with almost complete stenosis, and so the method was tried in a few of these advanced growths. In the first case the œsophagus was transected, the stomach end being closed, and the patient died from leakage of the malignant stump. In the next cases the œsophagus was left in continuity and a side-to-side anastomosis performed with the intestine. The first 2 survived and the second 2 both died from infection. Of those who survived, one lived five months in comfort and the other is still alive and standing his turn at the club seven months after operation.

¹Proc. R. Soc. Med., 1943, 36, 143.

(a) *As regards fitness for the operation*, it is often impossible to forecast accurately how a patient will tolerate the anæsthetic, and merely opening the abdomen or thorax or both. Once this has been done, it may be easier to estimate how much more the patient will stand. We have been forced to irradiate some operable tumours because we felt the patient would not tolerate wide resection, or even to abandon cases suitable for direct irradiation because the patient was faring badly. So we very rarely decide beforehand what form of treatment will be carried out, but prepare for all contingencies as far as possible.

(b) *As regards estimating the extent of spread* of the disease, laparotomy is essential, since the spread to lymphatic glands from the lower œsophagus and cardiac area is usually below the diaphragm, mostly to left gastric glands, partly to vasa brevia glands, and partly to pancreatic glands along the splenic vessels. Spread to the posterior mediastinum can be sought for when the thorax is opened. There is some difference of opinion as to when the laparotomy should be done, but it would seem to be unwise and unfair to the patient to open his thorax and divide his diaphragm, before we know the extent of spread in the abdomen.

(i) When there is well-marked œsophageal or cardiac obstruction, *gastrostomy or jejunostomy* may be necessary before the patient's condition can be improved sufficiently to stand the main operation. This can be done through a small upper left paramedian or rectus-splitting incision, through which exploration of the tumour and whole abdomen is possible.

(ii) In other cases, the abdomen can be explored through a similar incision a week or ten days before the main operation, as advocated by Garlock, or immediately preceding this latter as advised by Churchill and Sweet. We have usually followed this latter practice, so as to avoid two operations, but using a different incision more suitable for extension into the thorax.

When the best form of treatment can be decided upon beforehand, there are various methods of approach.

(1) For Resection

(a) *Transsthoracic, transdiaphragmatic approach* without doubt gives a good exposure of, and access to the lower œsophagus and upper stomach. The main principles are the same for all methods, with minor differences in technique as regards choice of level, resection of ribs, division of ribs, &c. The wound is relatively quick to open and close.

(b) *Abdominal approach* alone is usually considered inadequate for cardio-œsophagectomy, due to poor exposure of, and difficult access to, the operation field.

(c) *Two-stage operation* described by Marshall (1938). (i) *First stage* is done from abdomen alone, consisting of mobilization of the stomach with tumour and glands, which are all pushed up into the thorax through the enlarged œsophageal hiatus. (ii) *Second stage* is done from the thorax two weeks later, when the tumour and glands are removed and the anastomosis performed.

Angular abdomino-thoracic incision.—In our early cases, the abdomen was explored through a mid-line incision. When irradiation was decided upon, a transverse incision was made from the upper end of this, through the 6th and 7th left costal cartilages into the 5th space, round to the posterior axillary line. The thorax was opened and the diaphragm split down to the œsophageal hiatus, the incision skirting round the left edge of the pericardium. This gave good access to the cardiac area, though some difficulty was experienced in retracting the angular flap containing the divided left costal margin.

Oblique abdomino-thoracic incision.—In our later cases this difficulty was overcome by exploring the abdomen through an oblique incision across the upper abdomen, from about the 9th right to the 7th left costal cartilages, in line with the outer part of the 5th left interspace. This incision was continued through the left costal margin lower down into the 5th space, the thorax opened and the diaphragm divided as before. This gave a wide straight opening with much better direct access to the whole stomach and lower œsophagus. We have used it for direct irradiation and for surgical excision. But the main disadvantage of both these incisions is the time taken to open and close the wound. When irradiation is carried out considerable time is saved compared with that taken for resection. But then the patient is usually in a worse condition to stand a long operation.

(2) For Direct Irradiation

Due to the tendency of the growth to spread along the stomach or to lymphatics towards the mid-line or beyond, exposure must be made to enable the irradiation to be directed in an antero-posterior plan, otherwise uniform irradiation of the tumour area would be

tension. The stomach is a better organ to use than the small intestine both on account of its remarkable reach—right to the apex of the pleura, and of its indomitable blood supply—never so hazardous as that of a Yudin length of small gut. The stomach should first be made into a bed for the œsophagus to lie on, the bed is firmly sutured to the chest wall before the anastomosis begins.

As for the anastomosis itself, I believe its security depends entirely on the care the surgeon pays to details. It should be end-to-side, using interrupted fine silk sutures, in two layers. The layer most liable to tension is the anterior œsophago-peritoneal. It cannot be too often repeated that in the œsophagus the *mucosa* is the master-layer—just as in the stomach it is the seromuscular layer.

As for the results, the improvement in operative mortality has been remarkable. In 1940, the operation mortality for all the 191 cases of œsophagectomy collected by Ochsner and De Bakey was 72%. I have just heard their figures from three American surgeons—Garlock, Sweet and Phemister. The mortality for their total of 172 operations in the last few years is 29%. Out of 9 cases of this operation in the last five years I have lost 3. We have not yet recovered from the realization of the high malignancy of carcinoma of the œsophagus, but there are two redeeming considerations. First, the survival figures of the above three American surgeons suggest an eventual five-year cure rate of about 10%; secondly, in these latter years of rapid development there is no doubt that surgeons have done resections on a high percentage of cases which were not really operable. This has not only increased the operative mortality but has greatly reduced the proportion of long survivals. But, to say the least, it looks as if the results are going to be appreciably better than in cancer of the stomach.

Mr. Alan Shorter: Diagnosis.—The main accessory aids to diagnosis of carcinoma of the cardia and lower end of the œsophagus are: (i) Radiology; (ii) œsophagoscopy; (iii) gastroscopy.

Space allows me to deal only with radiology which is probably the most useful, but is not free from pitfalls. Special methods enable different diagnostic points to be demonstrated.

(a) *Barium swallow* in the erect position will show the site, type and degree of obstruction and the presence or absence of dilatation of the œsophagus above. This latter occurs to a great degree with carcinomatous obstruction more often than is generally appreciated, while it is usually a marked feature of cardiac achalasia. There the obstruction is not at the cardia but at the diaphragm or above (Calthrop).

(b) *Trendelenburg tilt* of the patient after the barium has entered the stomach will often show distortion or a filling defect of the cardiac stomach on the lesser or greater curvature especially, or of the abdominal œsophagus.

(c) *Retrograde barium meal*, by running barium into the stomach through a gastrostomy tube and then applying the Trendelenburg tilt, will show the cardiac area when the œsophagus is obstructed.

(d) *Air bubble*.—Stewart and Illick, and also Kirklin, stress the importance of examining the air bubble for deformity or the shadow of a soft tissue mass. This is done in the empty or partially barium-filled stomach.

(e) *Air filling*.—Wasch and Epstein have developed a technique of air filling of the stomach, with or without barium, for examining the anterior or posterior walls of the cardiac area. Tumours of these parts will sometimes not be shown by filling the stomach with barium and the Trendelenburg tilt.

Treatment.—At the present time surgery seems to hold out the greatest hope of cure, especially in the early stages. Every case is worth exploring, unless there are clinically obvious widespread metastases or the patient's condition is too poor. Surgical exploration is the only reliable way of deciding the correct form of treatment. Then, and only then, can we decide whether the site and type of tumour and the extent of spread permit of surgical removal, either curative or palliative. Cases rendered inoperable by the poor general condition of the patient or by irremovable local spread, we (Dr. Cranston Fairchild and myself, *Lancet*, October 27, 1945, p. 522) have been treating by a method of Direct Irradiation during the past two years. The object is to irradiate the tumour directly through the open wound, without other viscera or the body wall intervening, thus delivering a more accurate and effective dose of irradiation at high intensity directly to the tumour and field of local spread. We feel that it is more reasonable to irradiate most what most needs irradiating, i.e. the tumour and any local spread, and not the overlying skin and intervening vital tissues or viscera. That is where, in our opinion, external irradiation of visceral cancer fails.

So we feel the choice of treatment lies between Surgical Excision and Direct Irradiation. The problem is how best to decide which is the more suitable method for each individual case.

(a) *As regards fitness for the operation*, it is often impossible to forecast accurately how a patient will tolerate the anæsthetic, and merely opening the abdomen or thorax or both. Once this has been done, it may be easier to estimate how much more the patient will stand. We have been forced to irradiate some operable tumours because we felt the patient would not tolerate wide resection, or even to abandon cases suitable for direct irradiation because the patient was faring badly. So we very rarely decide beforehand what form of treatment will be carried out, but prepare for all contingencies as far as possible.

(b) *As regards estimating the extent of spread* of the disease, laparotomy is essential, since the spread to lymphatic glands from the lower œsophagus and cardiac area is usually below the diaphragm, mostly to left gastric glands, partly to vasa brevia glands, and partly to pancreatic glands along the splenic vessels. Spread to the posterior mediastinum can be sought for when the thorax is opened. There is some difference of opinion as to when the laparotomy should be done, but it would seem to be unwise and unfair to the patient to open his thorax and divide his diaphragm, before we know the extent of spread in the abdomen.

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Due to the tendency of the growth to spread along the stomach or to lymphatics towards the mid-line or beyond, exposure must be made to enable the irradiation to be directed in an antero-posterior plan, otherwise uniform irradiation of the tumour area would be

impossible. Therefore the left transthoracic approach is unsuitable for direct irradiation of these tumours.

Post-operative reactions have been no more severe than would have been expected after the operation alone, even after a maximum tumour dose of over 1,500 r in three minutes.

CASE I.—Male, aged 35. Carcinoma of lesser curve, 13 cm. long by 7 cm. antero-posteriorly by 4.5 cm. thick. Alive two years after direct irradiation.

CASE II.—Female, aged 57. Carcinoma of abdominal œsophagus 5 cm. long by 2.5 cm. wide. Lived fifteen months after direct irradiation, then died of bronchopneumonia and cirrhosis of the liver. No growth was found in treated area but a few deposits were found at base of right lung.

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Mr. Donald Barlow said that he had carried out ten resections of the lower end of the œsophagus with or without the stomach, and of these, four were still alive and well. One was for a simple stricture but all the others were for carcinoma.

He had found that especially in those cases where it was necessary to prepare a jejunal loop for anastomosis to the œsophagus, as, for instance, where most of the stomach was infiltrated by growth, the best exposure could be obtained by resection of the 10th rib on the left side perhaps with division of the posterior end of the 9th. This was an entirely new approach but it had three great advantages:

(i) Only the lower part of the incision need be made in the first place so that operability of the growth could be assessed before opening the chest and diaphragm.

(ii) As pointed out by Mr. Allison, resection of carcinoma of the stomach or œsophagus must include block dissection of all lymphatics and glands likely to be infiltrated. Those on the splenic artery and pancreas and around the pylorus, &c., were most important and in several of the speaker's cases not only the spleen and peritoneum on the posterior wall of the lesser sac but also the splenic artery and part of the pancreas had been removed. This exposure greatly facilitated this manoeuvre.

(iii) The preparation of jejunal loop after the manner of Yudin was made much easier and the arterial arcades could easily be transilluminated.

Whereas in one of the speaker's cases it had been possible by mobilizing the duodenum to bring it up into the chest to effect a direct œsophageal anastomosis, he had to prepare jejunal loops in three others. One of these patients was still alive and well. In another case in which it had been necessary to leave the distal two inches rather blue in order to get enough length, the operation was done in two stages, the loop being left below the diaphragm. When a week later the chest was opened to resect the œsophageal growth, the loop could not be found without opening the abdomen through a paramedian incision and the loop was discovered at the bottom of the pelvis with three inches of the distal end gangrenous. The surviving part of the jejunum had to be brought out subcutaneously and the upper end of the œsophagus through the neck. He had found in the third case where it was also necessary to leave the distal two inches of jejunum blue, that by bringing the loop subcutaneously at the first stage of the operation, it survived because it derived some additional blood supply from the tissues in which it was embedded. If desired he thought it might be possible at the second stage of the operation to remove the jejunum from its subcutaneous bed and bring it up through the diaphragm if its proximal end had already been threaded through the transverse meso-colon and up behind the stomach through the lesser omentum.

Mr. Barlow thought that a preliminary gastrostomy interfered with the operation and disagreed with another speaker that the phrenic nerve should not be crushed following an anastomosis in the chest because it was necessary to suture the stomach or jejunum to the opening in the diaphragm and unless this were done there would be drag on the anastomosis which would endanger its safety.

He considered it was quite useless to irradiate adenocarcinomas and failed to understand Mr. Tanner when he spoke of postural drainage for the treatment of pulmonary œdema. The speaker had found that where the patient was well enough, postural drainage might be useful where a lobe was atelectatic but in most instances it was advisable to pass a bronchoscope immediately and aspirate the bronchial contents, since failure to do this might result in many deaths.

Section of Neurology

President—J. PURDON MARTIN, M.D., F.R.C.P.

[January 3, 1946]

DISCUSSION ON CORTICAL ATROPHY

Mr. Harvey Jackson: The literature on the subject of cortical atrophy is disappointingly sparse. Certainly one would not do justice to this discourse without including those atrophic states of the cortex that accompany atrophy of subjacent white matter. Thus any condition attended by shrinkage of cortical tissue claims significance and warrants inclusion.

In referring to cortical atrophy two different forms of morbid anatomy come to mind. The one produces constriction of the affected gyri whilst the intervening sulci deepen and widen. The appearance of the cortex thereby resembles that of a shelled walnut enveloped in a fluid sac—appearances suggesting the terms “walnut brain” and “wet brain” as most appropriate designations. The second type of atrophic change is to be found incorporated with disease in the white matter. The gyri are flattened on the surface, widened transversely, but attenuated in depth of grey matter—well demonstrated in association with porencephalic cysts.

From the point of view of the neurosurgeon, the scope is perhaps more restricted, for, in so far as his practice is concerned, the effects of injury and the differentiation between tumour-formation and clinical states simulating tumour-formation are the main deliberations. Indeed the clinical material from which my cases are derived provides a number in which the precise pathological diagnosis of meningioma has brought me into the therapeutic programme.

Before discussing any of the more intimate details of particular lesions a more generalized citation of the many factors in causation is warranted. The order in which the various types of lesion are to be discussed has no application to their relative incidence; in fact some stress will be made of less common, though less frequently, recognized states.

Perhaps I may refer somewhat speculatively, and with trepidation, to the systematized atrophies, not without the full realization that the primary disorder may be a demyelinating process in deference to an atrophic state. It cannot be denied that such conditions as Schilder's disease and atrophy of the Pick, or Alzheimer type, occasionally stray into the hands of the neurosurgeon either because the true nature of the disease is missed in its early phase, or because of a less typical form of onset. In Schilder's disease the onset may be suggestive of a focal lesion and this can be accompanied by papilloedema. In so far as the generalized atrophies are concerned—patients are sometimes admitted in stuporose or semicomatose states. Under these circumstances, suspicion of the presence of a subdural hæmatoma may determine the surgeon into making exploratory burr holes.

The surgeon is ever mindful of the effects of injury, and is only too well aware of the possibility of diffused damage in addition to local injury. Moreover the initiation of diffuse changes from both closed and open injuries is appreciated. Strangely enough, while the dire effects of repeated head injury gain recognition the practical implication of this knowledge sometimes fails: the occurrence of atrophic changes in the brain originating from the occupation of boxing is well recognized, yet the extensive cortical atrophy that develops from the oft-repeated convulsive treatment, applied by psychiatrists to the relief of depression and other mental disorders, is ignored.

When talking of injury mechanical disruption of structure is the usual inference, but it must not be forgotten that other physical agents can be responsible. In particular I refer to X-rays. Occasionally one sees very extensive atrophic changes in the brain brought about by the application of intensive deep therapy for a cerebral tumour. The atrophy is of a very protracted onset, hence it is not to be seen with the more malignant gliomata owing to the short duration of life afforded by these neoplasms. It may be a matter of five years or more before the change materializes.

Those lesions thus far discussed have been of such a nature as to involve a number of gyri even when described as "localized" This by no means excludes the feasibility of an atrophic state applied to a portion of a gyrus. Doubtless an injury may be so restricted in effect, but the lesions to which I am about to refer are of other causation. They are the results of infection or of vascular disturbance of one form or another. Those infections most prone to produce what one supposes to be limited zones of "encephalitis" are the specific fevers—one has seen lesions that had arisen during the course of measles, whooping-cough, influenza, dysentery, tonsillitis, scarlet fever, pneumonia, &c. Patients who have been so afflicted seek advice on account of and relief from epileptiform manifestations, either focal or general. Unfortunately the import of infection in the clinical history may fail to gain recognition, and in consequence a patient may be submitted to an unnecessary exploratory operation. Similar patches of localized atrophy sometimes result from thrombosis of a cortical vein—a complication occasionally seen during pregnancy, or during the puerperium. Other forms of atrophic lesions are to be encountered, forms arising out of pathological vascular states. The diffuse cerebral atrophy of senile dementias consequent on chronic cerebrovascular disease is well recognized. A less heeded form of atrophy, vascular in origin, is that produced as the result of an arteriovenous fistula. Just how this takes effect is not established, but the anoxemic state of the blood is a probable factor. The mention of a vascular fistula reminds one that the large arteries which supply the brain can be directly involved in other ways, even in their extracranial course; an injury to the internal carotid artery in the neck has been known to cause extensive atrophic changes in the brain.

Omission of those peculiar atrophic states of the cortex to be found in babies, so beautifully depicted in an article by Ingraham and Matson (1944) under the title of "Subdural Hæmatoma in Infancy", would leave our discussion incomplete. The cortex in some of these cases shows an extraordinary state of formation of the affected area—this is described in that article as consequent on hæmatoma formation. How this change could be produced by the compression induced by a subdural hæmatoma is difficult of explanation. The pathology is obscure. In my opinion the state of the brain in some cases at least is more likely to result from structural defect of developmental origin. The frontal lobes and the parietal lobe, and the paracentral lobule in particular, seem to be sites of predilection (figs. 1 and 2).



FIG. 1.—Excessive quantities of air distributed over the frontal and parietal regions. A gross degree of cortical agensis.



FIG. 2.—Air over the surface of the parietal lobe of a baby indicating a restricted degree of agensis.

What are the clinical aspects of these several different conditions? Obviously the resultant disturbances are in some degree to be correlated with the particular regions of the brain involved. Nevertheless diffuse atrophic changes can occur without giving rise to localizing evidence manifest on neurological examination. The incidence of

epileptiform phenomena is very high—in something like 75% of all cases. Generalized convulsions occur, from frontal lesions in particular; Jacksonian attacks associate themselves with Rolandic lesions. Focal attacks appear to originate more commonly from the limited patches of encephalitis brought about by localized infection or circumscribed vascular thrombosis.

Whatever the form of the attack, in typical cases of cortical atrophy the history has proved generally to be a protracted one of several years' duration. A carefully elicited history should reveal any possible underlying infection, injury, or thrombosis recognizable as the exciting factor. When focal attacks have occurred over a number of years and then, on examination, neurological signs are judged to be static, tumour is unlikely. Should the neurological signs prove the lesion to be extensive, in terms of cortical implication, then, in the absence of symptoms and signs of intracranial pressure, the diagnosis of tumour would be improbable. Moreover the clinical state is often of a character that is difficult of explanation on a tumour basis; a poor mentality is not an uncommon finding, pyramidal signs are frequently accompanied by reduced sensory perception in one form or another, and in about 25% of my personal cases a visual field defect has been present.

Headache is a complaint in about 50% of cases but it bears hypotensive qualities as a rule, therefore it is unlikely to be mistaken for the headache of increased intracranial pressure.

Vomiting has not played any part in the clinical stories available.

Ultimately we reach the stage where a relatively circumscribed area of cortical atrophy becomes more or less indistinguishable from the development of a cerebral tumour, especially a meningioma. The history is that of a prolonged story of epileptiform attacks, periods of years not being unusual. The attacks are of focal or Jacksonian nature, usually to be followed sooner or later by paresis in one limb, and perhaps later still by hemiparesis. Indeed the whole story is that commonly supposed to characterize tumour-formation. Headache may, or may not, occur. Under these circumstances one may ask if a clinical differentiation between tumour and atrophy is to be reached. Personally I believe that such a differentiation is possible, but I would not care to base treatment on clinical evidence alone. Confirmatory evidence is not only advantageous, it is essential.

How then may this differentiation be formulated? In the first place one should keep the possibility of cortical atrophy in mind when a history of epilepsy of several years' standing is presented by an adult patient. The age-incidence is by no means restricted, although the majority of cases in my experience have been between 30 and 50 years of age. Evidence of a tendency to neurofibromatosis is usually lacking in atrophy, whereas it is not infrequent in a patient harbouring a meningioma. In what one considers to be a typical patient the blood-pressure tends to be on the low side of normal. Mentally these patients tend to be intellectually dull with poor memories and reduced powers of concentration should the atrophy be widely distributed. The optic discs most often are normal, visual acuity is normal, but field defects are surprisingly frequent. Usually the optic discs are within normal limits of appearance. However, on occasion one sees a peculiar moistness to be likened to that of the sclera and eyelids after weeping—an appearance aptly described as a "wet disc". The apparent swelling is not usually measurable.

Pathological investigation.—Lumbar puncture: Generally the manometric pressure of the cerebrospinal fluid is subnormal. Total protein and cell contents are normal. Wassermann reaction is negative. X-rays show no change.

Radiographic examination.—Plain X-rays so far as I am aware, cannot be said to show any characteristic appearances. Over and over again, however, I have been impressed by the rather exuberant pattern of the diploëic vascular channels in these cases. These vascular markings can be misleading for they may be incorrectly interpreted as supportive evidence of that adventitious vascularization we recognize as occurring in the presence of a meningioma.

Curiously enough the incidence of calcification in intracranial structures, e.g. pineal gland, choroid plexuses, and the falx, is greater than that occurring in normal patients of corresponding ages. Should any displacement of such shadows be recognizable, the displacement is towards the side of the lesion.

Owing to irregularities of bony density and occasionally from calcific deposits on the dura mater, one may observe a shadow, a shadow that may be acceptable as a hyperostosis, thereby being taken to confirm a diagnosis of suspected meningioma, whereas in fact no actual tumour is in existence. Careful elucidation of the nature of shadows of this type will necessitate stereoscopic films (figs. 3 and 4).

Even with the most careful study of radiographs it is obvious that mistakes can still be made. How then should one confirm the diagnosis? Contrast radiography by air



FIG. 3.

FIG. 3.—Patch of rarefaction (indicated by arrow) in the parietal region associated with subjacent cortical atrophy.



FIG. 4.

FIG. 4.—Bony irregularity (indicated by arrow) in the frontal region likely to be mistaken for a hyperostosis associated with meningioma formation. Note exuberant pattern of vascular channels.



FIG. 5.

FIG. 5.—Air diffusely distributed over the cortex, even over the parietal lobe—an indication of diffuse atrophic changes.



FIG. 6.

FIG. 6.—Visualization of the third ventricle on lateral view—considered to be incompatible with a normal brain.

encephalography or ventriculography usually proves conclusive. On carrying out such forms of investigation one may be astounded at the extent of the abnormality so envisaged.

Gross defects in radiographic appearances are easy enough to interpret, but just how much alteration in an X-ray is essential to confirm the presence of atrophy is uncertain. Estimations of the relative capacities of the ventricles and the subarachnoid spaces, up to now, have been rather conjectural, being formulated on previous observations extended over numerous cases. Impressions have led me to believe that accumulations of air over the parietal cortex are evidence of abnormality, especially if the exposures are made with the patient in a horizontal posture. Likewise visualization of the outline of the third ventricle on a lateral view is not to be seen in the undilated ventricle on the exposures ordinarily employed (figs. 5 and 6).

Evans (1942), in a recent paper, reports an investigation into the relationship between the transverse diameter of the anterior horns and internal diameter of the skull. Judging from his figures it seems that a ratio of not less than 1 : 3 must be looked upon as within normal limits.

Electro-encephalography in its present form does little more than indicate an abnormality, more often than not of wide distribution; sometimes lateralizing changes are available. According to Trowbridge and Finlay (1942), normal E.E.G. tracings may be found in cases showing only cortical atrophy, but are not found in cases with dilated ventricles.

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 TROWBRIDGE, E. H., Jr., and FINLAY, K. H. (1942) *Arch. Neurol. Psychiat.*, **47**, 931.

Dr. John J. Fleminger: During the years of this last war a diagnosis of cortical atrophy was made in 71 cases admitted to a neurosurgical unit for investigation. 31 of these were infants, and of the remaining adults, 28 were sent in by neurologists, all with a clinical diagnosis of cerebral tumour. Among these 28 cases there is a short series which appears to stand apart from the rest. In selecting these I have excluded all those cases in which there was anything in the history or on examination which might have pointed to a cortical degeneration, so that no case was included which gave any history of head injury, recent infection or with hypertension or arteriosclerosis, or was over the age of 60. This has left 12 cases, which appear to be examples of a cerebral atrophy of unknown cause, presenting clinically as cerebral tumours, and probably allied in pathology to the pre-senile dementias, but differing from these in that dementia is not found.

These cases consist of adults between the ages of 27 and 57 with an average age of 45. 8 were men and 4 were women. The commonest clinical diagnosis made was of a slowly-growing benign tumour, most frequently meningioma. In none was there anything to suggest any alternative pathology, and it was only on further investigation that the true nature of the condition was discovered.

There were certain very definite negative findings common to all of them. These were: normal fundi with normal optic discs, normal cerebrospinal fluid and fluid pressures, negative W.R.s, and the absence of any form of mental change suggesting dementia. In every case the blood-pressure was normal or low, and in no instance was there any bradycardia. Nausea and vomiting did not occur in any case. There was also no history of concussion or any other kind of craniocerebral injury as these cases had been excluded.

The most important symptoms were.—Epilepsy of all varieties, both major attacks and focal fits, motor and sensory; transient attacks of uselessness of a limb leading to paralysis; dysphasia, almost exclusively of the expressive kind; severe headaches and attacks of dizziness. When memory defect occurred, which was seldom, it was always associated with some degree of dysphasia.

Among the physical findings, loss of power in limbs was unilateral in every instance and the hemipareses were flaccid in only two cases; sensory impairment was less frequently found, but was most characteristically a loss of position sense. Ocular palsies and visual defects only occurred in 2 cases and homonymous hemianopia in one of these.

Straight X-rays of the skull revealed no constant or prominent abnormal features. In some the vessel markings over the vault were rather more evident than normal, and in one case, there was an area of irregular calcification corresponding to degeneration of the hemisphere discovered at craniotomy.

Electro-encephalography was done in only two of the cases. In both of these there was an abnormal focus in the region of maximum atrophy and in one, performed on a man with a left hemiparesis, the E.E.G. suggested a diffuse cortical dysfunction in both hemispheres, but most predominantly in the right frontal region. From these two cases alone it is obviously impossible to draw any conclusion as to the value of E.E.G. in the differentiation of this condition from tumour.

The discovery of cortical, or at least cerebral, atrophy was ultimately made by air studies or by craniotomy and direct inspection. A ventriculography was performed in each case, and some also had lumbar or cisternal encephalograms. The characteristic features of atrophy, as shown by air studies, in these cases were dilatation of the ventricles either bilaterally or unilaterally without any shift of the ventricular system, and, more striking, the increased convolutional marking of air in the subarachnoid space revealing the widened sulci, as seen in encephalograms. This was best seen over the vertex when the patient was X-rayed in the sitting position. Subdural puddles of air at the frontal and occipital poles and down the side of the falx were frequently seen, and were sometimes seen in the temporal region, in ventriculograms. In this connexion one should mention the increase in depth of the subdural space and the lax, sometimes wrinkled dura, found when the burr hole for ventriculography has been made, which were often the first indications that one was not dealing with a space-occupying lesion. One important fact is that although the physical signs and the symptoms may point to only a local cortical lesion, and in fact there may only be a unilateral ventricular dilatation, this is not always the case, and frequently the area of atrophy as demonstrated by air studies is seen to extend over a wide distribution and often to the opposite hemisphere.

The characteristic appearance of the surface of the cerebral cortex at craniotomy was a deep subarachnoid space bridging over widened sulci filled with excess of C.S.F. under low pressure. These sulci frequently, but not invariably, contained large thickened and tortuous blood-vessels. The cortex is described as being more rubbery and harder than usual to the touch and the convolutions appear shrunken and narrow. 4 of these cases had craniotomies, all performed by Mr. Wylie McKissock, and all presented a similar appearance, and also appeared to be macroscopically identical with other cases of atrophy of known cause.

The following are brief summaries of three of these cases which demonstrate some of the more typical features.

CASE I.—Man, aged 40. Admitted January 1946 with a six months' history, beginning with attacks of pins and needles in his left foot and weakness of his left hand. He was treated for rheumatism until he became so paralysed that he was unable to get about. He also complained of frontal headaches. He had a left lower facial palsy and a flaccid paresis of his left arm and leg without sensory loss. His ventriculograms showed dilatation of the whole of the right lateral ventricle compared with the left and increased convolutional markings over the cortex, particularly in the right frontal region, showing the maximum atrophic change to be in this area (fig. 1).

CASE II.—Woman, aged 56. She had a gradually increasing hemiplegia for two years, starting in the right foot and spreading upwards to involve the right arm. She complained of severe frontal headache. A diagnosis had been made of left frontal meningioma. Her ventriculograms showed dilatation of the left lateral ventricle compared with the right. A craniotomy was performed. A left fronto-parietal flap was turned down, and the typical appearances of shrunken atrophic brain were seen, maximum at the upper ends of the motor-sensory cortex. Now, five years later, this woman is still alive, moderately well, but has developed a severe spastic paraplegia.

CASE III.—Man, aged 27. Had major epilepsy for two years. A diagnosis of right frontal meningioma had been made; E.E.G. showed a right frontal focus of slow irregular delta waves. His encephalogram pictures showed increased convolutional markings in the frontal region. At operation marked atrophy was revealed in the right frontal region and unusually large and tortuous venous channels were seen (fig. 2). A year after he was discharged, he had shown no deterioration and his fits were being controlled by luminal.

The value of encephalography in this condition is demonstrated in figs. 3, 4, 5 and 6. They are of a man with aphasia and right hemiplegia. Ventriculograms, figs. 3 and 5, first showed dilatation of the left lateral ventricle. Then lumbar encephalography performed

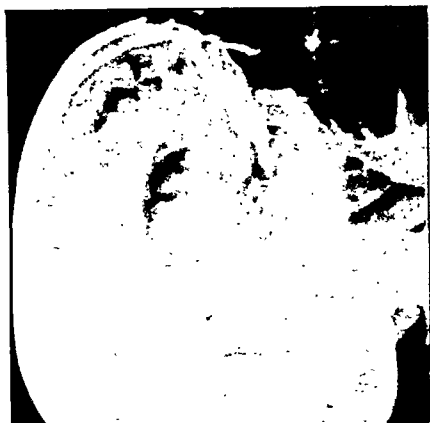


FIG. 1.

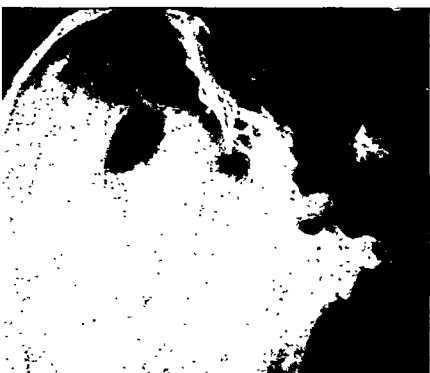


FIG. 3.

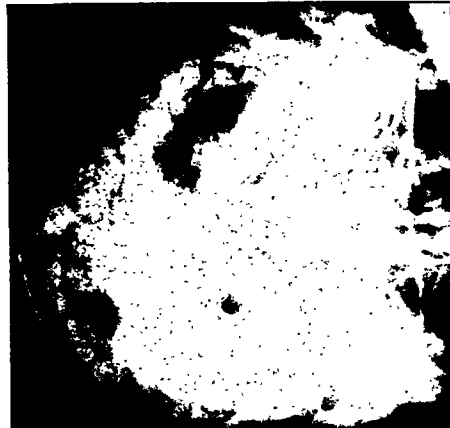


FIG. 4.



FIG. 5.



FIG. 2.

JOHN J. FLEMINGER: Cortical Atrophy.

FIG. 6.

about a week later revealed the condition of the surface of the cortex with the widened convolutional markings far more evident on the left than on the right, figs. 4 and 6.

The only light which can be thrown on the pathology of this condition from these few cases, is the report on a small biopsy that was taken from the cortex and underlying white matter at the operation on a man aged 37 with aphasia and right hemiplegia. As one cannot lay any stress upon an individual case, this does not contribute much to a discussion on ætiology; here, however, is a short summary of the report:

"Cortical degeneration and sclerosis of unknown ætiology. Two areas of scarring in the cortex in close proximity to blood-vessels. The nerve cells show marked swelling of the nucleus in many cases; others, however, are shrunken and dark staining with corkscrew apical dendrites, these cells being clearly in the process of chronic degeneration. The white matter showed increased gliosis with much perivascular hæmorrhage." The neuropathologists who saw the sections were unable to classify the nature of these changes.

SUMMARY

This has been an attempt to present a few cases which do appear to stand apart from other types of cerebral atrophy, at least in the way in which they are presented to the physician. That is, as a condition affecting adults of middle years with a symptomatology closely resembling a slowly growing cerebral tumour. The most important points which may assist in a clinical differentiation seem to be—the absence of papilloedema, bradycardia or vomiting even in very advanced cases. The ultimate distinction and diagnosis can only be made with certainty by air studies or craniotomy. As far as prognosis is concerned, only one of the 12 cases has, to my knowledge, died, but the follow-ups are too short for any really helpful conclusions to be drawn at this stage.

I have been unable to find any reference in the literature which bears directly on these cases.

Finally, I would like to express my gratitude to Mr. Wylie McKissock who has given me so much kind assistance.

Section of Odontology

President—LILIAN LINDSAY, M.D.S.Durham, L.D.S.Ed.

[February 25, 1946]

Unilateral Hyperplasia of the Mandibular Condyle

By MARTIN A. RUSHTON, M.B., L.D.S.

HYPERPLASIA of the mandibular condyle on one side only appears first to have been described by Adams before the Medical Section of the British Association in 1836 (Adams, 1873) as a manifestation of rheumatoid arthritis. Humphry (1856), Eve (1883) and Heath (1883) described further cases, and small numbers have been added by other authors from time to time. Surveys of reported cases then known were made by Heath (1884), Perthes (1907) and others, the most recent accessible to me being that of Gruca and Meisels (1926). By that time about 17 cases were known; and since then further examples have been reported by Ivy (1927), Dufourmentel (1927), Thoma (1945), and others. It may now be possible to add a little to the survey of Gruca and Meisels; and I am able to describe a few new cases.

CASE I.—The patient was a healthy soldier of 28 who complained of discomfort in the right temporomandibular joint (fig. 1). Spontaneous dislocation of the mandible began to occur there one year before; and when seen it happened every time the jaw

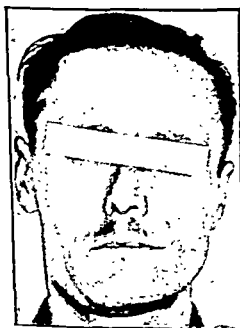


FIG. 1.

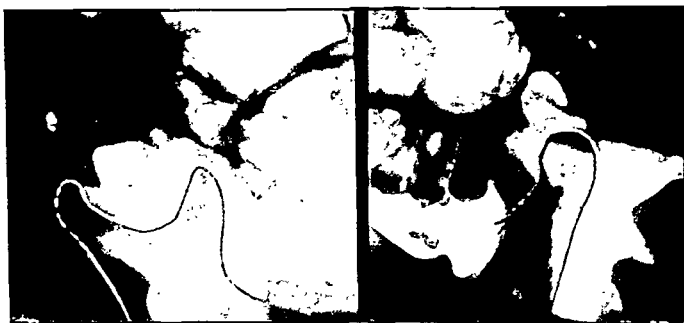


FIG. 2.

was opened and became reduced spontaneously on closing. Most of the usual signs of unilateral condylar hyperplasia were present: elongation of the ascending ramus on that side, and enlargement of the condylar neck and head but not of the coronoid process (fig. 2). There was an open bite of the cheek teeth on the same side and an

about a week later revealed the condition of the surface of the cortex with the widened convolutional markings far more evident on the left than on the right, figs. 4 and 6.

The only light which can be thrown on the pathology of this condition from these few cases, is the report on a small biopsy that was taken from the cortex and underlying white matter at the operation on a man aged 37 with aphasia and right hemiplegia. As one cannot lay any stress upon an individual case, this does not contribute much to a discussion on ætiology; here, however, is a short summary of the report:

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This has been an attempt to present a few cases which do appear to stand apart from other types of cerebral atrophy, at least in the way in which they are presented to the physician. That is, as a condition affecting adults of middle years with a symptomatology closely resembling a slowly growing cerebral tumour. The most important points which may assist in a clinical differentiation seem to be—the absence of papilloedema, bradycardia or vomiting even in very advanced cases. The ultimate distinction and diagnosis can only be made with certainty by air studies or craniotomy. As far as prognosis is concerned, only one of the 12 cases has, to my knowledge, died, but the follow-ups are too short for any really helpful conclusions to be drawn at this stage.

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main cartilage mass. The activity in the precartilaginous layer appears to regulate the rate at which the condyle and the condylar neck (which is formed from the condyle by remodelling) will grow. At about the age of 20 the formation of cartilage from precartilaginous tissue normally ceases and the replacement of cartilage by bone gradually stops also. The marrow cavity is now entirely shut off from the remains of the cartilage by a closing plate of bone. An inactive remnant of the precartilaginous layer persists, and might be stimulated to activity once more in certain circumstances, for example in acromegaly (figs. 3 and 4).

The sections of this abnormal case showed that the precartilaginous layer is in some parts of great thickness, at others less so, but apparently producing cartilage cells everywhere at its lower border. The cartilage itself is in parts very thick, and it is everywhere being actively eroded and replaced by new bone (fig. 5). Islands of cartilage can be recognized nearly 1 cm. below the main cartilage mass. The condyle was therefore in a state not only of active but also of irregular growth; and we may say that its excision has not merely cured the complaint but prevented the development of a more severe deformity later.

CASE II.—The following case was kindly referred to me by Mr. G. J. Parfitt and Mr. A. McLeod. The patient was a soldier of 36 who complained solely of the asymmetrical appearance of his face (fig. 6). The chin was projecting to the right and forwards and the vertical dimension of the mandibular ascending ramus on the left was abnormally great. The few remaining lower teeth on the right had come to occlude outside the upper teeth, and the left lower canine tooth lay just beneath the left upper central incisor. The appearance suggested that the whole lower jaw had been projected forward from the left condylar region. Movement was full and free. Radiographs showed that there was an enormous increase in the length of the left condylar process and increase in the size of the left condyle (fig. 7). The left coronoid process was no larger than normal and hence appeared relatively very short.

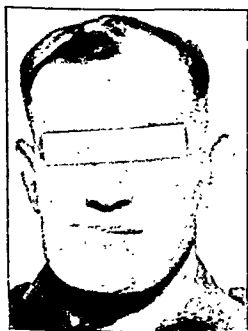


FIG. 6.



FIG. 7.

Asymmetry was first noticed at the age of 16, and it continued to increase, he thinks, until two years ago after which no change was noticed. He has never had a discharging ear or, according to him, any other illness. He started boxing at 15 and this became his principal interest.

It was decided to resect about 1½ in. from the left condylar region, leaving a false joint. This operation was performed by Mr. J. B. Cuthbert through the post-auricular approach, the enlarged condyle being removed after cutting through the rather soft condylar neck, and a portion of the latter also resected. It immediately became possible to restore the chin to near the mid-line and to reduce its prominence, so that the right lower incisors now occluded inside the upper. No fixation other than a bandage was used, and the latter was removed for meals after the third day, movement being encouraged. In two weeks a partial lower artificial denture was provided and the patient was discharged. Movements were painless and free but not completely full, and function was good. The improvement in appearance from the front was considerable, that of the profile very satisfactory indeed (fig. 8).

The secondary changes which occur in the mandible in the course of years as a result of condylar overgrowth are such that removal of the condyle cannot be expected to restore complete symmetry in an advanced case.

The condyle removed was of more than twice normal thickness but near normal width, and thus rather globular. Many small islands of calcified cartilage were present in the bone trabeculae. There was quite a thick layer of cartilage present on part of the articular

overclosed shearing bite on the other. The mandible was obviously tilted about an antero-posterior axis, but there was little deviation of the chin, probably owing to the deep incisor overbite. No history or signs of injury, or of middle ear or other disease could be obtained. Discomfort was immediately relieved by excision of the condyle (Dr. J. Converse).

Before describing the results of histological examination I shall describe the normal condition. During the period of growth the articular surface of the condyle is covered with fibrous tissue as Hertwig first pointed out (1892). Beneath this is a layer of pre-cartilaginous connective tissue, and it is from this that the next layer, of cartilage, is progressively formed. The cartilage becomes calcified at its lower part and is there eroded into bays continuous with the marrow cavity of the bone; and bone is deposited on, in, and around it. The older the individual the less cartilage islands can be found in the bone of the ramus; at birth they can be found at least as far down as the mandibular foramen, but at 16 years they will only be found a few millimetres from the

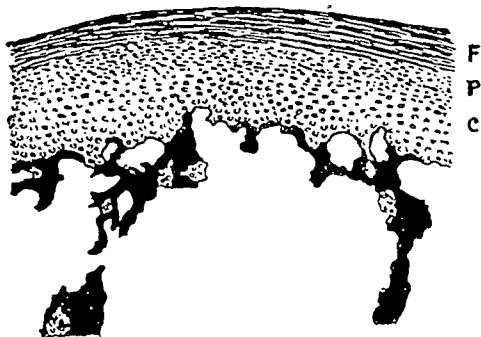


FIG. 3.—Normal condyle. Diagram of section at 16½ years. F, fibrous layer; P, precartilaginous layer; C, cartilage; bone black.



FIG. 4.—Normal condyle. Diagram of section at 21 years. A continuous bony plate has formed beneath the articular surface (Figs. 3 and 4 from *Brit. Dent. J.*, 1944, 76, 60).

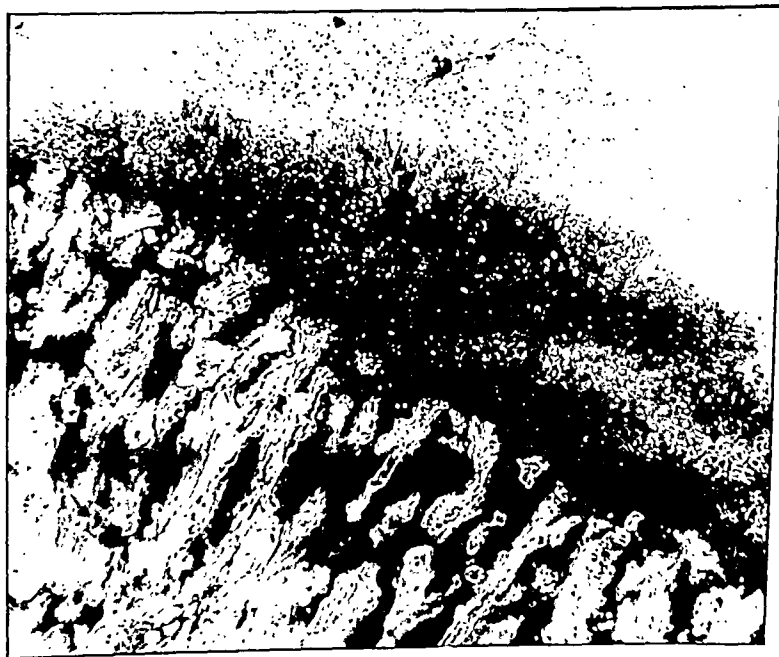


FIG. 5.—Stained picrothionin. $\times 50$. Precartilaginous tissue above; thick layer of cartilage (black); line of erosion bays; and beneath, numerous bone trabeculae (grey) containing much cartilage (black).

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surface, rather irregular in width and in the distribution of its cells (fig. 9). Growth, however, seemed almost to have ceased, and though several marrow bays protruded into the cartilage most of them had become lined with a layer of bone. The general appearance was one of inactivity supervening upon excessive growth, and this is in agreement with the man's belief that deformity had not increased for two years.

CASE III.—An officer of 24 complained of prominence of the chin on the right side which made it impossible for him to disguise himself. It was understood that the feature was known to the Gestapo and that he was due to return to enemy-occupied territory in a few weeks. He had first noticed the abnormality two years ago after an aeroplane accident in which, however, he had had no facial fractures. The left condyle occasionally became subluxated. Examination showed the left side of the mandible to be longer than the right, the condylar neck longer and the coronoid process relatively short. I could not determine whether the condyle was enlarged or not. The mid-line of the lower incisors at their crowns was to the right of the mid-line of the upper jaw, and at the apices still more so. The body of the jaw on the long side was less in its vertical measurement than on the short side. There was no clear evidence that the deformity was still progressing but the patient thought it was. Owing to the short time available Sir Harold Gillies decided to reduce the chin prominence by local excision of bone and to change the shape of the nose for good measure. The operations were done from within the mouth and nose respectively, so that no scars were visible.

If this case is correctly diagnosed as one of condylar hyperplasia the deformity is quite likely to recur.

I have re-examined the records of published cases, with the exception of a few recorded in theses and dissertations not directly available here [see table on opposite page]. There are 29 cases including my own.¹

Sex and age.—It appears that Gruca and Meisels were mistaken in supposing that the abnormality is more frequently found in women: 14 men and 12 women were affected in 26 cases. The right and left sides appear to be affected with equal frequency (R. 10; L. 12 in 22 cases). With regard to age distribution it is probable that the date when the abnormality was first noticed was usually several and sometimes many years after abnormal growth had commenced. However, taking the dates available we find that the most common time of discovery was between 15 and 30; and perhaps the abnormal growth usually starts to become significant between the ages of 10 and 25 (age-groups: 0—9, 3; 10—19, 8; 20—29, 9; 30—39, 2; 40—49, 1). Whether it usually ceases spontaneously at some age without operation is not at all clear. In my second case it appeared to be doing so at 36; in Gruca and Meisels' third case the patient at 49 could remember no increase of deformity; and in Heath's second case the deviation was said to have become arrested at 20 after the application of a blister and a course of potassium iodide.

The gross lesion.—In endeavouring to interpret the varied specimens which have been placed on record it is a help to consider what would be the effect of an increased growth-rate just beneath the condylar surface at various ages. In childhood we should expect the result to be a jaw of increased length on the affected side but without much other disproportion of its parts. It can be supposed that the mechanism by which the normal condyle is remodelled to form the neck is usually sufficient to prevent the formation of a much enlarged condyle in childhood, and the effect would be no more than an unduly rapid advancement of the bone in a direction away from the joint. Such a case would be very difficult to recognize as due to condylar abnormality at an early stage, since the upper jaw and other parts would accommodate themselves to the abnormal mandible. My Case III is perhaps a late example of this kind; and the following case may be an earlier example:

Boy 17½ years. He had received a kick on the lower border of the right side of the mandible at 11 years, causing a scar but no fracture. It had now been first noticed that his face was asymmetrical. The right side of the jaw was 1 cm. longer than the left, and it seemed clear that the right side was too long rather than the left too short. The mid-line of the lower incisors was misplaced a little to the left with respect to the uppers and the left canine had erupted outside the arch. The relationship of the first molars was normal on the short side but on the long side the lower molar was anterior to its normal relationship with the upper. Radiographs showed that the body of the long side of the mandible was smaller in its vertical measurement than the other, but little else abnormal. I have postponed decision in this case for one year to discover whether any further deviation will occur.

Another comparable case is that of Perthes (1922) in which the typical deformity had developed from the age of 12 until 16 when it was shown.

¹A further case has now been reported by H. G. Worman, C. W. Waldron, and D. F. Radusch (1946) *J. Oral Surg.* 4, 27; another by J. W. McNichol is in the press.

When the normal growth period of the mandible is drawing to a close an abnormal continuance of growth at the whole condylar surface would lead to the formation of an elongated neck (so long as the remodelling mechanism at the neck persisted) and then to an enlarged head. This result is shown in my Cases I and II and is a more common finding. But it may happen that the abnormal growth-rate continues at only part of the condylar surface, or faster there, with the result that a mass of bone and cartilage arising at that side of the condyle becomes mushroomed over it in such a way as to exclude it from the joint and to replace it as the functional condyle. This is well shown in

TABLE

Author	Sex and age when presented	Age when noticed	Side Deformity	Finding	Other disease
(1) 1836 Adams	F. 30	After 25	R. Much	Ramus asc. enlarged. and supracondylar mass. No cartilage. Autopsy	Rheumatoid arthritis of many joints for 5 years
(2) 1856 Humphry	F. 21	19	R. Much	Condyle enlarged 3 times. Knotty surface of fibrocartilage	None
(3) 1883 Eve (McCarthy)	M. c. 40	—	R. Much	Enlarged body of jaw and supracondylar mass. Autopsy specimen	Arterial disease. Deaf
(4) 1883 Heath (i)	F. 36	26	L. Much	Very large condylar mass, lobulated 1½ in. × 1 in.	Left hemiplegia at 25
(5) 1884 Heath (ii)	F. c. 20	c. 20	— Slight	"Hypertrophy of condylar neck"	None
* (6) 1898 Grube	F. 17	—	— —	Exostosis of articular surface; neck normal	—
(7) 1899 Eckert (Mikulicz)	F. 50	41	R. Much	Supracondylar mass size of small plum. Rest of jaw normal	None
(8) 1906 Eiselsberg (i)	M. 42	39	L. Much	Condyle size of pigeon's egg, lobulated	None
(9) 1906 Eiselsberg (ii)	M. 21	21	L. Much	Condyle enlarged, rough	None
(10) 1907 Riedel	M. Elderly	—	— —	Condyle bigger than a thumb	Deforming arthritis of many joints and trigeminal neuralgia
(11) 1907 Voelker 3 cases	—	—	— Much	Condyle size of walnut, ramus asc. elongated	None
(12) (13)					
* (14) 1919 Lohmann and Perthes	F. 21	20	— —	Condyle enlarged with anterior exostosis	—
(15) 1922 Perthes	F. 16	12	L. —	Jaw elongated, condyle said not to be enlarged	—
(16) 1926 Gruca and Meisels (i)	M. 24	13	R. Much	Jaw enlarged and supracondylar mass	Rt. otitis media at 10 years
(17) 1926 Gruca and Meisels (ii)	F. 21	15	R. Slight	Condyle and neck enlarged	Rt. otitis media at 11 years
(18) 1926 Gruca and Meisels (iii)	M. 49	Early youth	L. Much	Condyle enlarged, bent back	None
(19) 1926 Wermuth	M. 18	13	R. Much	—	Fell from roof at 12 years
(20) 1927 Ivy (i)	F. 35	32	R. Much	Condyle 3 cm. transverse diam., lobulated	—
(21) 1927 Ivy (ii)	F. 27	26	L. Slight	Condyle uniformly enlarged	—
(22) 1927 Dufourmental (i)	F. 24	18	L. Much	Condyle enlarged, neck elongated; osteophytes	W.R. positive
(23) 1927 Dufourmental (ii)	M. 25	24	L. Much	Condyle enlarged, neck elongated	W.R. positive
(24) 1934 Brodie	M. 19	c. 16	R. Much	Condyle "forward in its fossa"	None
(25) 1944 Rushton (i)	M. 28	27	R. Moderate	Condyle and neck uniformly enlarged	None
(26) 1945 Rushton (ii)	M. 36	16	L. Much	Condyle enlarged and neck very long	None
(27) 1945 Rushton (iii)	M. 24	22	L. Slight	Left jaw and condylar neck elongated	None
(28) 1945 Thoma (i)	M. 37	Childhood	L. Moderate	Condyle very large, jaw not much elongated	Lt. otitis media
(29) 1945 Thoma (ii)	M. —	Childhood	L. Much	Condyle enlarged and ramus elongated	None

*Marked in List of References.

McCarthy's specimen (fig. 10) which Eve interpreted in the same sense, observing further that since the rest of the jaw on the same side was also enlarged the abnormality probably commenced in early life. We do not know when deformity was first noticed in this case, but in a closely similar case published by Gruca and Meisels it was already noticed at 13 years. The original case of Adams appears to have been of the same kind (fig. 11), and the so-called exostosis on the medial side probably represents the remains of the original condyle. The deformity here was supposed to have followed an acute rheumatic



FIG. 9.—Stained Azan. $\times 75$. Fibrocartilage above; then precartilaginous layer, interrupted on right; then hyaline cartilage in which two erosion bays are still active; below, continuous layer of bone (black).



FIG. 8.



FIG. 11.



FIG. 10.



FIG. 12.



FIG. 13.

attack at 25, due to living in a damp cabin, but the increased length of the whole posterior part of the jaw on that side and the compensatory downgrowth of the opposing maxilla seen in the lithograph of the skull suggest a commencement some ten years earlier.

It seems likely, however, that in some cases abnormal growth does not begin until the normal growth-period of the jaw has ended. Thus in the famous case of Heath (fig. 12), in which there was enormous overgrowth of the condylar head without remodelling to form an elongated neck, the ramus ascendens and the rest of the jaw were of normal size. And in the well-known case of Mikulicz (fig. 13) described by Eckert (1899), in which deformity was not noticed until the age of 41, it appears (if we can rely on his drawing) that the whole mandible including the condyle was normal except for the extraordinary bony growth from the latter's antero-medial aspect. The fact that here the exostosis did not become mushroomed over the original condyle may mean that it was not in this case formed through a cartilage stage, as indeed the bone at the extreme edges of a normal condyle is not. Eckert says it had an ivory character.

Ætiology.—The association of the deformity with rheumatoid arthritis in the first case (Adams) naturally led to its attribution to that disease, but the subsequent cases already led Heath to doubt this explanation in 1884, and in fact the association appears only once to have been repeated (Riedel, 1907). Arthritic changes noted only in the joint itself (Humphry, 1856; von Eiselberg, 1906; Dufourmentel, 1927) may well have been secondary. An association with hemiplegia in Heath's first case invited the suggestion that neurotrophic effects were responsible, but no support has been provided by other cases. Inheritance and familial distribution have not been known to occur. Intra-uterine malposition (Lohmann, 1919) would be rather unlikely to affect the ramus ascendens, not then formed, more than the parts of the jaw then present or formed in the early years of life; and birth injuries would not cause excessive but restricted growth. Many cases investigated for syphilis have shown no evidence of that disease. Cruca and Meisels' observation of an association with homolateral otitis media in two of their three cases has not been repeated, though it may have occurred in McCarthy's case (*see also* Thoma, 1945). A history of trauma has been uncommon, but blows on the jaw are so universally experienced that no significance can be attached to their mention or otherwise. Eve (1883) considered that the abnormality might well be of the nature of congenital gigantism and pointed to the late development of enlargement in some cases of gigantism of the limbs.

It is certainly true that in cases of unilateral partial gigantism affecting both jaws and the teeth and neighbouring structures there may be enlargement of the condyle and increased height of the ascending ramus on that side (Barwell, 1881; Keith, 1923). However, in all such cases the facial deformity has not been a late development but has been noticed very soon after birth; indeed the fact that the size of the teeth has been affected implies a very early commencement of the deformity.

In the cases discussed in this paper the centre of disturbance appears very localized and probably confined to the condylar cartilage in the first place, though the zygomatic arch sometimes appears thickened.

In several respects the disorder is comparable with the single cartilage-covered exostoses of the long bones. These, according to Geschickter and Copeland (1931), are most commonly discovered between the ages of 10 and 25, which agrees well with the common age of discovery of condylar hyperplasia. Both occur at sites where precartilaginous tissue exists and persists throughout a great part of life; and the structure of both is similar except for a greater tendency to lobulation in the exostoses of the long bones. The factors of trauma and infection which are believed to be instrumental, among other causes, upon the long bones are equally applicable to the jaw. The principal differences appear to be that in the case of the jaw the excess of bone is often remodelled to subserve a functional purpose, that no sex difference is so far apparent in the mandibular cases, and that (so far as I know) malignant change in them has not been recorded. The circumstance that in the temporo-mandibular joint alone does the exostosis occupy the articular surface can be explained on the ground that this joint differs from others in its origin and structure.

Treatment.—Excision of the condyle has long been known to be most successful (*cf.* Humphry, 1856); and the alternative procedure of resecting part of the body of the jaw can only be advisable in cases which are no longer progressive. After condylectomy it is important to see that the patient does not return to the old bite which, as Eckert and others have noticed, has become comfortable for him and even the only position in which mastication is possible; this may entail the extraction of some teeth and the provision of

artificial dentures. Gruca and Meisels wrote: "The earlier the operation is done, the smaller the deformation will develop in the upper jaw and position of the teeth . . . the earliest resection of the articular head is not only advisable, but even absolutely indicated." But there are two difficulties: the first is to be sure at a very early stage that the deformity is progressive; and the second is that condylectomy at such a stage might make that side of the jaw permanently too short. The right course is, probably, to wait until the progressive nature of the deformity is beyond doubt, and until a point has been reached at which condylectomy will leave the two sides approximately equal.

I am indebted to the surgeons mentioned, and to Professor W. Newcomb for sections cut in his department at Park Prewett Hospital, E.M.S. The photomicrographs were made by Mr. T. W. Pearce and Mr. E. B. Brain.

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Section of Psychiatry

President—G. W. B. JAMES, C.B.E., M.C., M.D., D.P.M.

[March 12, 1946]

DISCUSSION ON THE VALUE OF PLAY THERAPY IN CHILD PSYCHIATRY

Dr. Margaret Lowenfeld: To be successful a discussion upon anything must be based upon agreement as to the meaning of the terms to be discussed. It is worth while, therefore, to consider the meaning of the four words in the title.

The word **PLAY** is usually associated with children, but it has a very much richer meaning than that and is commonly used in four senses, all of which go to make up the content of Play Therapy rightly understood.

The word **play** as commonly used in English has four meanings: Play as the opposite of work; Play in association with "games"; Play as it is used in the theatre; and Play in connexion with observation of natural objects, the play of light and shade, for example, and in connexion with instruments, play the piano, the playing of an orchestra.

The essential of the first use is the doing of something for the enjoyment one gets out of it; of the second, the carrying out of a social activity whose essential characteristic is the obedience of all players to prearranged rules. In the third use, the word becomes for the first time serious, and is the presentation of someone not oneself, while the play played by the player presents the author's attitude to men and women, his view of right and wrong and his personal reaction to his personal experience.

The fourth use is curious, it is the use of a mechanical instrument, a piano or a violin to express experiences which cannot be rendered in any other medium, and in which, even if the subject matter be given, the "meaning" given to that subject matter is personal to the player. If we are to use this word correctly as a description of therapy, all four qualities should be included.

To pass to the word **CHILD**, in common speech this word occurs in reference to all ages from about 3 to school-leaving age. The words "infant and toddler" preceding it, and "adolescent" or "young person" succeeding it. On the other hand, when the word occurs in mental hospital statistics, it commonly connotes an age of 16 or 17, and many discussions on matters concerning the children come to grief through lack of preliminary agreement as to the age range which is being discussed.

PSYCHIATRY is a term which originated with adult medicine, and has only comparatively recently come to be applied to children. This is a dangerous process as few concepts, customary and valuable for purposes of description of adult phenomena, can be safely transferred as they stand to children and this is no exception.

The essential of the concept of adult psychiatry is that it is based upon a behaviour criterion. Applied to children this led, quite naturally, to the selection, apart from rare cases of unmistakable psychosis in individuals under 20, of children who failed to conform to the adult conception of correct behaviour, and child psychiatry originated with Healy and Bonner's work on delinquents. Leaving the defectives on one side as falling into a separate class, consideration of delinquent children came to be extended to those unable to show adequate educational progress, to behaviour difficulties within home and school and only in a small part to children with difficulties within themselves. But the scope of modern psychiatry is far wider than this, and includes the psychoneuroses, psychosomatic disorders, and the study of personal anomalies of development. Should not the same range be included in child psychiatry? The value of any form of therapy cannot be assessed adequately until we know to what cases it is proposed to be applied.

With the word **THERAPY** we come to the heart of our problem. What is the goal we are to set before ourselves in child psychiatry? We find ourselves in a curious position. Child psychiatry is in a pre-Krepelin stage of development. Clinical description is the basis of medicine, whether that be psychological medicine or any other. Where are we

to find the clinical descriptions and the systematized psychopathology upon which child psychiatry is to be based? Are we interested in the child himself, and in what study of the child can tell us of the nature of human beings and of the possibilities latent in man? or do we agree with a recent writer that "First and foremost come environment, the parent and the home, then the teacher and the school" . . .? Are we to set as our goal the adjustment of the child to his environment, taking that environment as a given factor, or are we to aim at the development of the potentialities of the individual child? Until we have come to some agreement as to the goal of our work, we cannot estimate the value of any technique that we employ.

Associated with this problem is that of the individual who is to carry out the therapy. If we read carefully Mr. Alexander's Minutes of the Child Guidance Sub-Committee of the Association of Education Committees, we find that "diagnosis and treatment" of the whole range of difficulties occurring in children both at school and at home from the ages of 2 to 18 are to be carried out by "a fully qualified educational psychologist capable both of diagnosis and treatment." When we look further to see what form of training is going to equip such an individual, we find that psychiatry does not appear at all. In Mr. Alexander's view, therefore, the difficulties of children arise in spheres other than those covered by child psychiatry.

Within the field of medicine the views of those who practise child psychiatry range from those of Mrs. Klein and her group of pupils, who demand a very long and highly specialized form of training occupying many years, to those of a recent writer who described her training in the following terms: "Play is the language of children. They know it but we must either recollect it from our childhood memories or acquire it through analysis of ourselves and observation of the child. It is our patient who must help to re-educate us." In certain clinics the practice has grown up that if play is carried out as therapy it should be under the charge of a social worker, but in no case, so far as I have been able to discover, is this accompanied by any suggestion that the social worker should have a training in child psychology, child psychopathology or child psychotherapy.

We now come to the question of play therapy as a technique. There are four types of such therapy. First comes restitutive play. All children need room to run in, a secure atmosphere to play in, earth, air and water to experiment with and enjoy, and things to make and to do. Some children can accommodate themselves to what they get others become ill through the deprivation of these opportunities which modern civilization makes inevitable. Restitution of such elements is a powerful therapy. To make this type of play effective, the right sort of building is necessary, appropriately equipped. With the right people in charge this kind of play can sometimes have a magic effect, but we need to be clear that this is not the magic of psychiatry but of nutrition, the giving back to a starved child essential elements for growth.

The second type is play in groups with the objective of observation of the social behaviour of the children and to give assistance in their social adjustment. The greater the psychotherapeutic experience and understanding of the people in charge, the more likely it is that the group will be able to bring about in the children who take part in it lasting changes in behaviour. But, unless the group is in charge of someone with training and experience in child psychotherapy, this is not a psychiatric method, and non-technical play clubs can show parallel results.

The third type is the play therapy which deals with feeling and phantasy.

Now the feelings and phantasies which underlie neurosis take place within the personality of a patient, and unless he can be induced to tell us about them and has the skill to make himself intelligible, we cannot help him. It is hard enough for adults to convey feelings in words and for children quite impossible. To attempt therefore to do direct psychotherapy with children, whose language is action, without a knowledge of play and without opportunity for the child to express himself in play, is like attempting to treat an adult patient with whom we do not share a common language. It is this difficulty and the lack of adequate understanding of the structure of children's play, and particularly of the fourth form of play therapy, which brings about the confused transference phenomena with children which create so much of the difficulty in this form of treatment. The essential of play, used in this sense, is to put within the reach of children means by which they make clear to themselves and to us their inner experiences of feeling and phantasy: what use is made of the material produced depends upon the theoretical views and technical experience of the adults in charge of the work. The criteria of usefulness is the same in this, as in all forms of clinical medicine; that is, the suitability for treatment of the cases selected, the clarity with which the goal to be achieved is envisaged and the skill of the technician using it.

We now come to the fourth type of play therapy which is my particular contribution, and which I have decided to call direct projection therapy in order to distinguish it from other forms of play therapy, as both its basis and technique are different.

It has been my wish for a long time to achieve something more permanent in the nature of a record of the interior mental and emotional processes of children than the fluidity of play permits. I want to be able to carry away from a play session permanent statements in concrete objects which can be stored for study, much as the preparations in a pathological museum can be stored, so that the personal element can be reduced to a minimum and the records studied scientifically apart from the child, thus enabling progressive comprehension of the phenomena and their objective comparison with each other. I have given fifteen years to this attempt and have succeeded in devising instruments which make this type of permanent objective record possible, and have available over 1,000 cases of children and young adults studied in this way by myself and the group that works with me.

A major aim of this technique is to minimize as far as possible the factor in treatment which is dependent upon the personal equation and the relationship to the adult worker. Each child goes through a regular routine which is clear and definite in the mind of the therapist, but widely flexible in regard to the child. It is also devised to give the child as quickly as possible a feeling of being in a new atmosphere and in a world of his own. For example, the child on arriving for his first visit is greeted by some member of the staff trained in child psychotherapy, and while particulars are being taken from the accompanying adult, is welcomed to a part of the building set aside for children, presented with the mosaic test and asked to make something he likes. It is then explained to the child that what he does in the playroom remains between him and the psychotherapeutic worker and will not be reported upon at home. From then on the child is encouraged to make use of as many of the technical, objective, recording methods as he is inclined to use. There are, for example, hexagon mosaics, kaleidoblocs, design units, on the one hand, and 'world' material, town planning material, &c., on the other, supplemented with verbal methods such as the newspaper game, sentences, &c.

A running commentary is kept up as the child works, making him aware of what he is doing as he does it; but the deeper significance is not interpreted to the child until it emerges unmistakably from his work. In this way what appears is a presentation in which an object, a thought about an object, the same object in quite a different light—perhaps inside out—the essential meaning of the object to the child, and perhaps a puzzle concerning the teacher's name for the object, can all be presented together. Other observers seeing this material are interested in what can be brought about through interpretation of the objects in terms either of their affective meaning or their place in a pre-known theory of the mind. My interest is in the reason why exactly those objects appear at that time and place and arranged in that exact way.

The characteristic of this material is its difference from what one had expected. What is being dealt with in direct projective therapy is not primarily feeling, though feeling comes in later as a consequence of conceptions formed, but the processes of formation of early concepts, of these records of sensation, and the systematization of personal experience which each individual child makes for himself. In U.S.A. Eric Homburger Erickson has been exploring the same region, and Margaret Mead in her recent anthropological study of the people of Bali bases her work on his findings. Schilder's and L'Hermite's work on the body image is relevant to what appears, and much that other workers have done on thought forms in schizophrenia. That is to say that study of a long series of this type of objective production has brought to light a region of human experience as yet uncharted and undescribed. A strange characteristic of it is that there is in it neither time nor space, sequence nor direct causality. What it appears to me we have found in this region is, as it were, the prodromal form, the first or primary form, of thought, and for this reason I have suggested it be called the primary system. As the infant and young child has no frame of reference outside himself, or tool with which his experience can be shared with and checked by the experience of other people, each child has to make his own system of grouping and storing experience, and this becomes the basis of his approach to life. If either his actual experience is usual or his senses no more keen than those of his fellows, then he will sooner or later find words, poems, stories, games, which echo his interior experience, and enable him to pass through it and to make adequate contact with the external world, expressing himself in and through it. If, however, something goes wrong, if he becomes languid, ill, fails to take interest in his school work, fails to want to grow up, odd in behaviour, withdrawn, aggressive, peculiar, then what is happening is that the conclusions he has come to in his interior world are so different from his external experience, so frightening in consequence, that he remains sunk in it and cannot emerge to make contact with outside life.

If, however, working with him we can bring to his aid the facts I have discovered about this part of the mind, with their help discovery can be made of the inter-relatedness on other planes of the objects he presents. The grip upon his mind of these, as

to find the clinical descriptions and the systematized psychopathology upon which child psychiatry is to be based? Are we interested in the child himself, and in what study of the child can tell us of the nature of human beings and of the possibilities latent in man? or do we agree with a recent writer that "First and foremost come environment, the parent and the home, then the teacher and the school" . . .? Are we to set as our goal the adjustment of the child to his environment, taking that environment as a given factor, or are we to aim at the development of the potentialities of the individual child? Until we have come to some agreement as to the goal of our work, we cannot estimate the value of any technique that we employ.

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We now come to the fourth type of play therapy which is my particular contribution, and which I have decided to call direct projection therapy in order to distinguish it from other forms of play therapy, as both its basis and technique are different.

necessary to have a wide range of material. Sand, water and clay are the three essentials. With these a child will create whatever it wishes. But figures of men, women, children and animals, that permit of the dramatization of the world in miniature, lend themselves admirably to the needs of the child and often simplify the therapist's task of interpretation. Pencils, charcoal, chalks and paints appeal to the majority of children and are most effective where the expanse of paper and the quantities of paints are both large. It is always an advantage if the child feels constrained neither by the atmosphere of the interview nor the limitations of the play materials, but this does not mean an uncontrolled and uninhibited display, whether destructive or not. Such an eventuality could only occur with an unskilled and inexperienced worker.

So far I have only considered play therapy of the individual child. Treatment of more than one child at a time by the therapist has been tried, with varying degrees of success. Unfortunately it has often been regarded as an easy and harmless form of play therapy, open to the less experienced worker, whereas the converse is probably nearer the truth. In my view group therapy, with or without the aids of play material, or dramatic participation, is only effective in a residential establishment, whether hostel or school. The therapist must live with, and therefore be a living part of, the group. To avoid confusion it is probably wiser mainly to restrict the use of the term play therapy to treatment of the individual child.

To recapitulate:

Play therapy is a form of psychotherapy in children utilizing play material as its principal instrument. It is carried out by a therapist having a defined and conscious purpose, namely cure of a disability. The term should be used in no other context.

The technique, and the form of play material, vary with different workers, but fall mainly into one of three types: (a) Passive association and observation; (b) active interference through the play material; (c) verbal interpretation of the play activity.

The play therapist treats the child and should therefore be, or work in connexion with, a child psychiatrist. A lay play therapist forms a valuable, if not essential, addition to the usual Child Guidance team.

Play therapy, like all psychotherapy, is skilled work requiring exceptional personality endowment and prolonged training. The organization of a professional association of play therapists and the formulation and recognition of standards of training are much overdue.

[April 9, 1946]

DISCUSSION: PREFRONTAL LEUCOTOMY WITH REFERENCE TO INDICATIONS AND RESULTS

Professor F. L. Golla: The limited time at my disposal can best be filled by considering, in their broadest outlines, the specific effects of the operation of Moniz on the total personality, in the hope that some basis may be formed that will clear the way for a discussion of its therapeutic applications.

The time is not yet ripe when some of the more objective methods can be used to explore these fundamental considerations. "Il est suranné de penser anatomiquement" was the motto that Grasset printed on the title-page of his *Neurology* and though one can hardly expect our friend, Alfred Meyer, to agree with such an extreme functional attitude, I am sure that he would join in deprecating adventures in speculative physiological anatomy not based on experiment. On the other hand, the results of experimental work on the higher apes are not readily applicable to the elucidation of psychological disturbances affecting the least systematized of mental activities. At first sight, one might hope for help from the electro-encephalogram, but the day is not yet when the study of cortical potentials has reached a stage allowing the formulation of a systematic analysis of sub-cortical activities, however confidently we may hope that by some such method an ultimate elucidation of the somatic concomitants of mental activity may be possible.

It is in terms of descriptive psychology that our study must be prosecuted until the time arrives when it may be possible to reinforce psychological inquiry by physiology and the success of our psychological approach will depend on the use of holistic rather than analytic methods.

Let us first clear the ground by dismissing the consideration of the alleged impairment of reasoning as a sequel to the operation. Without going into detail, one may justify this attitude by pointing out that there are a sufficient number of cases in which bilateral

individual, "mad," unrelated, terrifying objects, relaxes, and energy begins to flow through this system to the outside world.

In attempting to describe this region shortly in words, I find myself in a position as difficult as would be that of a pathologist asked to describe actinomycosis without the aid of slides, preparations or drawings. Perhaps the essential aspect is the light this study throws upon psychosomatic conditions in children and upon the genesis of schizophrenia and psychopathic personalities.

In practice all four forms of therapy interweave with each other, and in the Institute of Child Psychology no child or group of children is treated by any one exclusively. It is for this reason that we ourselves feel that a minimum of three years' training, together with a year on the staff and a personal analysis, is necessary for those who would take up the play psychotherapy of children, but we feel that, with this background and correct equipment, play therapy and direct projective therapy form a flexible and delicate technique for the study and treatment of children suffering from the whole range of complaints covered by child psychiatry.

Dr. Alan Maberly: The time would seem opportune for making an attempt to define the nature of play therapy, its place in child psychiatry and the training and status of play therapists. I suggest that the term play therapy should be restricted to a form of individual treatment of children suffering from maladjustment or behaviour disorders involving neurotic disability. It is psychotherapy utilizing play as a principal means of treatment. This is not to say that play may not in other circumstances be constructive and even, in a sense, therapeutic, but it should not be termed play therapy unless the therapist takes an active and essential part.

Play enters into child psychiatric practice in many aspects, apart from its therapeutic purpose proper. For all small children, and some up to adolescence, actions speak more clearly than words, and the therapist must be familiar with every form of symbolism in play whether as a dramatized phantasy or in body language.

We may therefore consider the first function of play as a method of communication. It offers a means of quickly establishing a positive rapport with the child and at the same time opens up a productive path for further investigation. Few children can use words happily to express their feelings, even with adults who are familiar to them, and with strangers self-consciousness and artificiality are inevitable. Play is at once a defence against, and a retreat from, personal contact, which makes free expression possible if not easy.

In so far as establishment of contact with the child is a first essential step in the therapeutic relationship, this first function of play may be regarded as a part of play therapy, but strictly speaking therapy begins when the therapist enters into the play, of set purpose or not. It is important to realize that the child will gradually incorporate an adult into its play, whether or no the latter intends this to be so. Complete passivity on the part of the observer makes no difference—it only makes it easier for the child to attribute to the adult whatever feelings, whether of approval or of blame, he may expect or desire. One might in this way be presumed to approve an action or attitude expressed in the play of which one has no understanding. To this extent a so-called play therapist, untrained and without insight, may achieve a good result by observing the golden rule of a well-intentioned masterly inactivity. But it is not possible to say that such a technique can never do harm, and the ignorant healing the sick is no less inappropriate than the blind leading the blind. The above example, however, illustrates what one may describe as the first of the three principal techniques of play therapy, free play on the part of the child in the presence of a play therapist who remains passive, but in positive relationship with him. Without a positive relationship by which the child senses a friendly and sympathetic understanding, nothing can be achieved at all. Secondly, the therapist can *enter actively* into the play situation, either by a dramatic impersonation, or by interference with the pieces in the game, changing relationships, introducing new figures or removing existing ones. Thirdly, the therapist may *interpret* the meaning of the play to the child so as to bring to consciousness purposes and conflicts that have remained hidden or subconscious. The interpretation may relate to the play as such, or to the child's relationship and behaviour to the therapist.

It is clear that these three methods are in no way mutually exclusive, and all three may be utilized in certain cases either consecutively or simultaneously.

Some therapists lay great stress on the type and variety of play material available, while others attempt a certain uniformity and standardization. I do not think it is possible to generalize, and different workers will develop methods that they themselves find most effective, but to deal with children of all ages and all grades of ability it is

necessary to have a wide range of material. Sand, water and clay are the three essentials. With these a child will create whatever it wishes. But figures of men, women, children and animals, that permit of the dramatization of the world in miniature, lend themselves admirably to the needs of the child and often simplify the therapist's task of interpretation. Pencils, charcoal, chalks and paints appeal to the majority of children and are most effective where the expanse of paper and the quantities of paints are both large. It is always an advantage if the child feels constrained neither by the atmosphere of the interview nor the limitations of the play materials, but this does not mean an uncontrolled and uninhibited display, whether destructive or not. Such an eventuality could only occur with an unskilled and inexperienced worker.

So far I have only considered play therapy of the individual child. Treatment of more than one child at a time by the therapist has been tried, with varying degrees of success. Unfortunately it has often been regarded as an easy and harmless form of play therapy, open to the less experienced worker, whereas the converse is probably nearer the truth. In my view group therapy, with or without the aids of play material, or dramatic participation, is only effective in a residential establishment, whether hostel or school. The therapist must live with, and therefore be a living part of, the group. To avoid confusion it is probably wiser mainly to restrict the use of the term play therapy to treatment of the individual child.

To recapitulate:

Play therapy is a form of psychotherapy in children utilizing play material as its principal instrument. It is carried out by a therapist having a defined and conscious purpose, namely cure of a disability. The term should be used in no other context.

The technique, and the form of play material, vary with different workers, but fall mainly into one of three types: (a) Passive association and observation; (b) active interference through the play material; (c) verbal interpretation of the play activity.

The play therapist treats the child and should therefore be, or work in connexion with, a child psychiatrist. A lay play therapist forms a valuable, if not essential, addition to the usual Child Guidance team.

Play therapy, like all psychotherapy, is skilled work requiring exceptional personality endowment and prolonged training. The organization of a professional association of play therapists and the formulation and recognition of standards of training are much overdue.

[April 9, 1946]

DISCUSSION: PREFRONTAL LEUCOTOMY WITH REFERENCE TO INDICATIONS AND RESULTS

Professor F. L. Golla: The limited time at my disposal can best be filled by considering, in their broadest outlines, the specific effects of the operation of Moniz on the total personality, in the hope that some basis may be formed that will clear the way for a discussion of its therapeutic applications.

The time is not yet ripe when some of the more objective methods can be used to explore these fundamental considerations. "Il est suranné de penser anatomiquement" was the motto that Grasset printed on the title-page of his *Neurology* and though one can hardly expect our friend, Alfred Meyer, to agree with such an extreme functional attitude, I am sure that he would join in deprecating adventures in speculative physiological anatomy not based on experiment. On the other hand, the results of experimental work on the higher apes are not readily applicable to the elucidation of psychological disturbances affecting the least systematized of mental activities. At first sight, one might hope for help from the electro-encephalogram, but the day is not yet when the study of cortical potentials has reached a stage allowing the formulation of a systematic analysis of sub-cortical activities, however confidently we may hope that by some such method an ultimate elucidation of the somatic concomitants of mental activity may be possible.

It is in terms of descriptive psychology that our study must be prosecuted until the time arrives when it may be possible to reinforce psychological inquiry by physiology and the success of our psychological approach will depend on the use of holistic rather than analytic methods.

Let us first clear the ground by dismissing the consideration of the alleged impairment of reasoning as a sequel to the operation. Without going into detail, one may justify this attitude by pointing out that there are a sufficient number of cases in which bilateral

individual, "mad," unrelated, terrifying objects, relaxes, and energy begins to flow through this system to the outside world.

In attempting to describe this region shortly in words, I find myself in a position as difficult as would be that of a pathologist asked to describe actinomycosis without the aid of slides, preparations or drawings. Perhaps the essential aspect is the light this study throws upon psychosomatic conditions in children and upon the genesis of schizophrenia and psychopathic personalities.

In practice all four forms of therapy interweave with each other, and in the Institute of Child Psychology no child or group of children is treated by any one exclusively. It is for this reason that we ourselves feel that a minimum of three years' training, together with a year on the staff and a personal analysis, is necessary for those who would take up the play psychotherapy of children, but we feel that, with this background and correct equipment, play therapy and direct projective therapy form a flexible and delicate technique for the study and treatment of children suffering from the whole range of complaints covered by child psychiatry.

Dr. Alan Maberly: The time would seem opportune for making an attempt to define the nature of play therapy, its place in child psychiatry and the training and status of play therapists. I suggest that the term play therapy should be restricted to a form of individual treatment of children suffering from maladjustment or behaviour disorders involving neurotic disability. It is psychotherapy utilizing play as a principal means of treatment. This is not to say that play may not in other circumstances be constructive and even, in a sense, therapeutic, but it should not be termed play therapy unless the therapist takes an active and essential part.

Play enters into child psychiatric practice in many aspects, apart from its therapeutic purpose proper. For all small children, and some up to adolescence, actions speak more clearly than words, and the therapist must be familiar with every form of symbolism in play whether as a dramatized phantasy or in body language.

We may therefore consider the first function of play as a method of communication. It offers a means of quickly establishing a positive rapport with the child and at the same time opens up a productive path for further investigation. Few children can use words happily to express their feelings, even with adults who are familiar to them, and with strangers self-consciousness and artificiality are inevitable. Play is at once a defence against, and a retreat from, personal contact, which makes free expression possible if not easy.

In so far as establishment of contact with the child is a first essential step in the therapeutic relationship, this first function of play may be regarded as a part of play therapy, but strictly speaking therapy begins when the therapist enters into the play, of set purpose or not. It is important to realize that the child will gradually incorporate an adult into its play, whether or no the latter intends this to be so. Complete passivity on the part of the observer makes no difference—it only makes it easier for the child to attribute to the adult whatever feelings, whether of approval or of blame, he may expect or desire. One might in this way be presumed to approve an action or attitude expressed in the play of which one has no understanding. To this extent a so-called play therapist, untrained and without insight, may achieve a good result by observing the golden rule of a well-intentioned masterly inactivity. But it is not possible to say that such a technique can never do harm, and the ignorant healing the sick is no less inappropriate than the blind leading the blind. The above example, however, illustrates what one may describe as the first of the three principal techniques of play therapy, free play on the part of the child in the presence of a play therapist who remains passive, but in positive relationship with him. Without a positive relationship by which the child senses a friendly and sympathetic understanding, nothing can be achieved at all. Secondly, the therapist can *enter actively* into the play situation, either by a dramatic impersonation, or by interference with the pieces in the game, changing relationships, introducing new figures or removing existing ones. Thirdly, the therapist may *interpret* the meaning of the play to the child so as to bring to consciousness purposes and conflicts that have remained hidden or subconscious. The interpretation may relate to the play as such, or to the child's relationship and behaviour to the therapist.

It is clear that these three methods are in no way mutually exclusive, and all three may be utilized in certain cases either consecutively or simultaneously.

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It is true that restoration may be incomplete and it is certain that it will be carried out by other and more circuitous and clumsy systems of reference. So much may be premised seeing that we are dealing with an interruption of important nerve tracts. I do not know when the process of reintegration ceases any more than I know when we cease to profit from new experiences, but in a case that I have been observing daily for the past eighteen months the process is still going on. And this leads to the last point that I wish to make: Just as the indications for and against leucotomy must be based not on psychiatric classifications of mental disorders but on a study of the emotional subjective self in relation to the total personality, even so must the operation be considered only as a step in the reintegration of personality.

Without due concentration on psychotherapeutic after-treatment, results will often be disappointing.

Friends must be warned that the period of post-operative therapy may be a lengthy one and the physician must be prepared to devote considerable time to the instillation of a sense of responsibility by exploring with the patient such avenues to emotional ethical valuation as may yet be open.

Dr. Walter Freeman and Dr. James W. Watts (from the Department of Neurology, George Washington University. Paper read by Dr. Walter Freeman): *Pain of organic disease relieved by prefrontal lobotomy.*—Among the four hundred patients with mental disorders whom we have treated by prefrontal lobotomy a considerable number have had unbearable pain as the outstanding complaint. We felt justified, when the pain disappeared after lobotomy, in speaking of the relief of mental pain (Freeman and Watts, 1942a). In these cases the complaints of pain appeared excessive and out of proportion to the local condition found on examination. It was equally obvious that we were dealing with individuals who suffered greatly from anxiety, nervous tension, depression of spirit and fear of the future. To them, the sensation was more than pain, it was pain coloured by their gloomy outlook and by the supposed consequences of the pain. Every time the sensation occurred, it meant that something was going to happen or was in process of happening that meant more suffering to come. Sometimes the pain became symbolic of the torment and suffering that the individual recognized as the consequence of previous acts which still aroused feelings of guilt. "This dreadful pain", the agitated old lady would say, "I have only myself to blame for it. I'm on fire. If only my mother had cautioned me against masturbation! I can't go on living this way."

It seems that when the emotional component is reduced, when the feelings of guilt, the regrets for the past and the fears for the future are abolished, the sensations no longer have the same meaning for the patient. We recall an emaciated middle-aged woman (Mrs. C. H.) who had complained of pain in the back of twenty-eight years' duration. Her stomach "went into knots" on the slightest provocation. During the operation under local anaesthesia the patient complained bitterly about her back and her stomach, but paid little attention to what the surgeon was doing. While conversing with her, the neurologist laid his hand lightly upon her scaphoid abdomen and could feel a freely movable mass, probably the pylorus of a greatly ptosed stomach. The patient objected to this, begged him to remove his hand. As the surgeon severed the final quadrant in the frontal lobe the complaints disappeared and with them the palpable mass. In the year that has elapsed since the operation the patient has increased from 79 lb. to more than 100 lb. and has never again complained of either her back or her stomach.

Prefrontal lobotomy relieves anxiety and emotional tension in rather specific fashion. It diminishes concern over consequences. It eliminates the fear of pain. Pain may be present, but when it no longer arouses a mental picture of future disability and all that this may mean in terms of disaster to the person and his family, the experience can be borne with equanimity. Consequently, prefrontal lobotomy lends itself well to the relief of conditions in which the affective component of a painful disorder is equally important with the local condition.

Prefrontal lobotomy has not been used to any considerable extent for the relief of pain in non-psychotic individuals. Usually when medical measures fail to bring relief, the surgeon has severed nerves or spinal roots, resected part of the sympathetic system, or, in extreme cases, has performed anterolateral chordotomy. Sometimes such operations have been gratifying in the extreme, but sometimes, also, they have failed to bring relief. De Gutierrez-Mahoney (1944) has resected the post-central gyrus for the relief of persistent pain, but VanWagenen is the only one to our knowledge who has performed prefrontal lobotomy. The observation is unpublished, but concerns an individual who suffered pain in a phantom limb that defied multiple amputations. The relief was complete.

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A somewhat uncritical application of the Jacksonian concept of "levels" has been invoked as furnishing some support to the view that leucotomy removes the latest acquired inhibitory level. I can only say, without qualification, that I know of no observations that support this interpretation. In Bristol we have endeavoured, with a team captained by Dr. Hutton, to make an intensive study of the effects of the operation on those elements of the total personality that had not undergone demonstrable impairment as a result of the mental disorder. We have obviously had to limit such a study to a small number of selected cases; those in which there is reason to assume that some degree of irreversible deterioration has taken place are, of course, useless.

Let us first consider the immediate effects of leucotomy on the special type of subject that we are investigating. The first and most superficial impression of the post-leucotomy personality is that its possessor exhibits a purely objective mentality.

The subject responds readily and appropriately to variations of the environmental conditions, but seems to take little interest in remoter possibilities.

In no sense, however, can he be said to be deficient in prevision so long as prevision is concerned with the foreseeing of objective and not of subjective changes.

His emotional reactions to appropriate stimuli, directed to cause objective changes in the environment, are to all appearances normal.

Fear, anger and affection may be manifested within normal limits.

In such favourable cases, husbands or wives, friends or business associates, may detect little change from the prepsychotic personality.

At most, the subject may be a little ruder and less sensitive to the feelings of others; sometimes, but by no means often, a trifle more lazy or self-indulgent.

All this is, however, the outward manifestation of a far more radical change.

It is not until one has succeeded in gaining an intimate knowledge of the mentality of these subjects that it becomes apparent that in the early post-leucotomy period we are dealing with personalities exhibiting an impairment of the power of ethical valuation.

Their conduct is, as a rule, irreproachable for, even more than normal people, they are sensitive to the conditioning imposed by their upbringing; they are also acutely aware of the sanctions incurred by transgression of the moral codes. We find them, however, relieved of all sense of personal responsibility and of anxious self-questioning as to the ethical rightness of their conduct.

If one presents to them, for their judgment, problems in behaviour, their verdict will be that of conventional morality but their ethical judgments are determined by purely objective criteria untinged by emotional concomitants.

Man alone of living creatures can feel responsibility for his actions for man alone possesses the power of self-objectification.

This last-developed mental function depends on the integrity of the last-developed structure of the cerebrum, the prefrontal lobe in its relation to the thalamic system of emotional resonance. It is in those disorders of the personality in which we can detect disturbances of this system leading to anxiety states, so often characterized by obsessional conduct, that leucotomy is most successful.

Were this the whole story of leucotomy, grave indeed would be the responsibility of the physician who recommends it, for he must then envisage the substitution of a soulless robot for the insane patient.

Though I am far from denying the gravity of the decision, I think that to put the matter thus is to ignore a very important qualification.

What we tend to forget, or, to put it more offensively, what most of the crude mechanists who teach physiology never let us learn, is the almost infinite lability of the central nervous system. It is not the rigidly departmentalized system analogous to a telephone exchange, dear to the writers of textbooks, but, as the experimental work of Graham Brown and Sherrington, of Lashley and of Weiss, and the clinical observations of Goldstein, have shown, a flexible organic whole which if it cannot arrive at its goal directly will do so by another and less direct path.

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This patient did not survive long enough to test adequately our theories concerning the relief of central pain by prefrontal lobotomy; but the immediate result as far as reaction to manipulation of the painful limb was highly suggestive.

CASE IV.—V. S., a white woman, aged 50, complained of intolerable pain and burning upon urination with vesical tenesmus day and night, reducing her to a trembling, weeping invalid. The pains had developed subsequent to operation for prolapsed intervertebral disc during which there was accidental trauma to the roots of the cauda equina. Local procedures, such as re-exploration and removal of more tissue from the disc, resection of the presacral nerve, repeated injections of procaine into the tissues about the neck of the bladder and intraspinal injections of thiamin chloride produced no relief. No local cause for the pain was ever discovered, and neurologic examination disclosed no abnormalities of muscle power, reflexes or sensibility.

After more than a year, during which the only relief obtained was by increasing doses of morphine, prefrontal lobotomy was carried out under local anaesthesia. At first a minimal operation was done, severing only the fibres in the vicinity of the fasciculus cinguli, with the result that the complaints ceased on the operating table. They returned within two days, however, and a week later the operation was revised, severing fibres in all four quadrants in the frontal lobes, with permanent relief of pain. This patient has been followed for nearly two and a half years, and while she has presented many disagreeable personality features, she has made no complaints of pain.

When she was asked about the pain shortly after operation, she replied: "Sure. It's exactly like it was before".

"But you don't complain any more", we suggested.

"What's the use", she answered, "I can't do anything about it so it doesn't do any good to complain".

This patient has gained 55 lb., has needed no narcotics, but when interviewed recently she stated that while she felt no pain, "every drop of urine feels like a barrel". There is moderate urinary frequency about which the patient makes facetious remarks, but her distress vanished at the time of operation and has never recurred.

CASE V.—L. S., a 44-year-old white woman was first seen in November, 1936, at which time she had spent two years in bed because of "arthritis". There was moderate lipping of the vertebrae, but no other significant changes. However, the patient complained so bitterly and was so apprehensive that it was impossible to make any headway in treatment. She had a long history of abdominal operations for adhesions, maybe a dozen in all, was of subnormal intelligence and hysterical temperament. Prefrontal lobotomy was carried out by the Egas Moniz technique November 30, 1936. Within three days the patient permitted manipulation of the limbs. She winced and cried out when the knees were straightened, and the crepitus was very considerable, but instead of shrieking with apprehension and refusing to co-operate she showed interest and willingness to help in the efforts that were made to aid her. On the fourth post-operative day she walked with assistance, and the following day, on attempting to walk unassisted, she fell and sprained her ankle, but nevertheless kept on walking. Her whole reaction to pain seemed to have been altered in that the fear of being hurt no longer upset her emotionally. It has now been nearly ten years since her lobotomy and she has supported herself in adequate fashion in a book-bindingery. When she is asked about her sensations she puts on a long face and tells how terribly she feels, how much her back hurts, how she can hardly walk; and yet she never complains of these sensations to members of the family. (Freeman and Watts, 1942b.)

SUMMARY

Five cases are reported in which prefrontal lobotomy was performed for the relief of pain which had proved refractory to other methods of treatment. In all cases the pains were severe, constant and disabling. In all cases there was considerable structural basis for the pain, yet the emotional component, the emotional response to the pain, seemed to be more disabling than the pain itself.

Previous observations had indicated that when unbearable pain, psychalgia, is one of many symptoms of a mental disorder, prefrontal lobotomy relieves the pain along with the nervous tension and other emotional manifestations. The present cases indicate that when pain due to organic disease becomes unbearable and the fear of pain becomes as dreadful as the pain itself, prefrontal lobotomy is a desirable procedure.

Psychosurgery alters the individual's reaction to pain without materially changing his ability to feel pain. Pain may be present, but when divorced from its implications— insecurity, disability, guilt, death—it then becomes bearable and may be accepted with fortitude.

The speaker demonstrated the principles and surgical technique of prefrontal lobotomy by means of a sound film in technicolour prepared by The Psychological Cinema Register, Pennsylvania State University, Pa. This film dealt with the marks on the skull, the tracts severed at operation and the various surgical details of the procedure of prefrontal lobotomy of the so-called standard type in the plane of the coronal suture.

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We are reporting our experiences with prefrontal lobotomy in the relief of pain from recurrent carcinoma, tabes dorsalis, thalamic syndrome, trauma to the cauda equina, and hysterical contractures.

REPORT OF CASES

CASE I.—T. P., a 45-year-old white man, developed carcinoma of the rectum in 1942 which recurred in 1944 with severe pain in the perineum and down both legs. Anterolateral chordotomy was performed on both sides, with the production of analgesia on the right side but not on the left. In spite of this, the patient continued to suffer severe pain on both sides. Metastases occurred to the liver and lungs, with a great deal of abdominal pain which could be controlled only partially by morphine every three hours. The patient was in precarious condition, suffering constantly, unable to eat or sleep with comfort. His anticipation of pain was also pronounced. Even as he was being given a hypodermic he would say: "When the effect of this morphine wears off, you won't let me suffer, will you, Doctor? You'll give me another hypo, won't you?" He begged the nurses to give him something for his misery, saying that he was going to die anyway and might at least be given comfort. The emotional reaction to pain in this case seemed to be of such great significance that prefrontal lobotomy was proposed to him and he accepted it with relief, "anything you can do to ease this pain will be a blessing".

Prefrontal lobotomy was carried out April 27, 1944. Following operation the patient was dull and confused for a brief period but acknowledged his comfort, and no longer demanded morphine. In fact very little sedation was required and for a period he gained somewhat in ability to eat and sleep. With the progress of the disease the liver became more and more enlarged until it practically filled the abdomen. As long as the patient was not disturbed he voiced no complaints, but if he were moved, or the hand was placed on the abdomen he grimaced with pain. The analgesia to pin-prick was exactly as it had been before the lobotomy. Even his reaction to the inevitability of death seemed to be altered. Asked if he knew he was going to die, he replied: "Sure, everybody has to die, don't they?" This fortitude in the presence of pain and impending death continued until his demise August 1, 1944.

CASE II.—W. P., a 50-year-old white man, had been under treatment for tabes dorsalis since 1934. He had undergone malaria treatment and prolonged chemotherapy thereafter, so that the spinal fluid had become entirely normal. Nevertheless the pains persisted. The patient was of a rather worrisome type, thin, restless and anxious. He made a good income from driving a taxicab, but had to spend as much as \$60 to \$80 a week for morphine injections which gave him the only relief he could secure. As long as he remained completely quiet at home the pains did not bother him, but any activity seemed to excite them. Here again, anticipation of pain seemed to be the disabling factor in his condition. "I guess I could stand the pains if it weren't for the thought of them coming on". Domestic difficulties were also a source of distress to him, and prevented earlier carrying out of the proposed operation. Meanwhile one of his comrades in suffering, also a tabetic, committed suicide. The patient's family finally consented. Prefrontal lobotomy was carried out on December 4, 1944. Narcotics were discontinued. He continued to have attacks but he described them as twinges and he never complained about them. Because of the domestic situation and his lack of ability to care for himself adequately he was admitted to St. Elizabeth's Hospital and there is making himself useful to other patients in the ward. In the year that has passed since operation he has gained considerable weight, but the signs of tabes are as obvious as ever. His perception of pain is as keen as before, but his reaction to pain lacks the emotional component that was disabling. His euphoria is decreasing and his sense of responsibility growing so that he is allowed out of the hospital on extended visits.

CASE III.—L. McL., a 55-year-old white woman, red-headed with a corresponding disposition, suffered in childhood from rheumatic fever with resulting mitral stenosis. Embolism of the right renal artery occurred in 1932, with recovery after nephrectomy. In October 1939 she suffered cerebral embolism with resulting paralysis of the left side. Recovery was gradual, but beginning six weeks after the stroke she suffered disagreeable pains centring about the left side of the neck and running down into the fingers. The pains were aroused by any muscular activity, and particularly by emotional outbursts which were fairly frequent. They quieted down during relaxation and did not interfere with sleep. Examination showed weakness and spasticity of the affected limbs, with hyperextensibility of the fingers. Pinching, scratching and chilling with ice were unendurable. There was marked loss of the sense of position in the fingers. Since the arm could not be manipulated without provoking the hyperpathia and arousing emotion verging on rage, this patient had to live in very secluded fashion. After more than two years' ineffectual treatment prefrontal lobotomy was carried out on June 16, 1943. For the first two days she was drowsy and unresponsive; then she developed abdominal rigidity and distension and winced and cried out when the lower abdomen was palpated. She permitted manipulation of the left arm, and reacted only mildly to scratching and the application of cold. Death occurred on the fourth post-operative day from peritonitis due to a ruptured diverticulum of the sigmoid.

Examination of the brain showed the surgical lesions opposite the genu of the corpus callosum filled with clotted blood and friable material. The old infarct destroyed the bulk of the putamen and caudate nucleus, sparing the insula, thalamus and globus pallidus. In the thalamus, however, the centrum medianum on the right side was completely atrophic, the nucleus ventralis anterior and anterolateral parts of the nucleus medialis dorsalis showed moderate degeneration; and the dorsolateral part of the nucleus ventralis lateralis was partly degenerated. The right pes pedunculi was quite small and markedly degenerated in its medial portion.

this group were vertical incisions above the orbital cortex, the difference being that one was made half a centimetre deeper into the brain substance than the other. 35% of the 26 made good improvements, 5 of the 9 cases with good results were schizophrenics with some depressive features and two others were melancholics. According to our investigations this vertical incision is the lowest that can be made without significant hæmorrhage if a leucotome is used.

TABLE II.

	Good	Fair	Poor	Died	Total
Upper	15%	42%	41%	2%	52
Middle	11%	32%	53%	4%	71
Horizontal... ..	20%	33%	44%	3%	30
Lower	35%	42%	23%	0%	26
	17%	37%	43%	3%	179

One of the two incisions not included in the series was a lower vertical and horizontal combined, the other a cut parallel to the orbital cortex in a plane 15 to 20 degrees below the horizontal. Our experience of these is small as yet.

From an analysis of the results so far obtained it appears that the symptom of depression is best relieved by a lower incision, that the aggression of the catatonic may improve from a high incision and the paranoid schizophrenics may derive most benefit from the middle vertical combined with a horizontal incision. As yet it is too early to speak with any real assurance about these findings as the numbers are small for comparison and we have been tending to make lower and lower incisions in better and better patients.

The clinical differences produced by the middle and orbital incisions are very noticeable, although there is only about $\frac{1}{4}$ cm. difference in level between the lowest points of the two circular cuts. With the lower there is more headache, drowsiness, a disinclination to eat, restlessness, transitory neurological signs such as incontinence, irritability and upgoing toes, usually a more rapid pulse-rate and for the first four or five post-operative days there is considerable difficulty in assessing how much improvement the patient may eventually make.

By way of complications we have had 5 deaths. 4 from hæmorrhage and 1 from pneumonia, all occurring in the first 83 patients. With a gas, oxygen and ether anæsthetic there have been no deaths in the last 103 cases.

Three patients have had a single fit, a fourth two. One patient has been incontinent of urine since her operation but she is aware of it. One patient developed marked apathy for six weeks after operation and is clearing up slowly.

In conclusion I think we may first say that by using a minimal incision to avoid deterioration, very satisfactory results may be obtained from chosen patients even if they have failed to react to the other forms of treatment. Secondly, the effects of the lower incision appear to be better than the remainder particularly if there is a depressive element in the illness.

We wish to thank Dr. F. Reitman for his help and suggestions; he has been associated with us in the latter part of the work.

Dr. L. C. Cook: Among those with practical experience of leucotomy there is no doubt as to the important place it must take in our present armamentarium of treatments. Nevertheless, some recent criticisms, although manifestly ill-informed and actuated by deeply rooted unconscious antagonisms, may be useful in curbing the enthusiasms of the more impetuous exponents of physical methods in psychiatry. The risks of leucotomy are such that it should never be regarded as a routine method for any condition, and personally I should not care to take the responsibility of advising the operation for any patient I had not had under close observation, preferably as an in-patient, for a considerable time.

Experience has taught us that leucotomy is of greatest value in relieving states of morbid emotional tension and distress, and disrupting the behaviour patterns dependent on them, and that it is not a specific remedy for any particular mental disorder.

For convenience of classification likely candidates for this treatment may be placed in four groups:

- (1) Depressive psychoses with severe agitation and apprehension, in which convulsion treatment has failed or is contra-indicated.
- (2) Obsessive-compulsive states, where anxiety and rumination are of a grave degree of severity.
- (3) Some florid schizophrenic reactions with distressing hallucinations and delusions, and heightened affect.
- (4) Long-standing violent conduct disturbances associated with increased mental tension, occurring mainly in catatonic and paranoid-hallucinatory schizophrenia, but also in some aggressive psychopaths, encephalitics, epileptics and mental defectives.

Dr. E. Cunningham Dax and Mr. E. J. Radley-Smith: We mentioned our first two cases of section of the lower part of the frontal lobes in 1943 but a more detailed description is found in Hoffstatter, Smolek and Bush's article (1945, *Arch. Neurol. Psychiat.*). It will be seen that in this present paper the positions of the brain sections methodically work down to the orbital cortex.

Briefly there is evidence that the orbital cortex, perhaps together with a portion of the temporal lobes, forms a functional unit which may be called the emotional cortex. Work by Legros Clark, Earl Walker and Meyer has shown the extent of the anatomical representation of the orbital cortex in the thalamus, and its clinical importance has been emphasized by Spatz, Rylander and others.

There are two particular points we would like to make which may be of interest. First that the approach to our last 130 cases has been made through the temporal fossa thereby giving a landmark for a constant plane of section. Secondly that we have always used a Macgregor-Crombie leucotome, with the definite intention of dividing a comparatively small number of fibres, hoping thereby to avoid the signs of deterioration described after the use of the more extensive operation.

The temporal approach is made from a point 3 instead of the usual 6 cm. above the zygoma, thereby allowing the Sylvian vessels to be seen as a landmark in every case. From this point different sections can be made both vertically and horizontally by varying the depth of incision and the direction in which the leucotome is pointed.

We have made bilateral incisions in this way in nine different positions, in the main on disturbed patients of long history.

The position of the sections has been worked out on fresh post-mortem material prior to operation. This was done by marking the brain through the drilled skull with coloured dyes according to the points at which the leucotome should be directed, sectioning the removed brain through the dye marks and making tracings against which the leucotome could be laid and the sections drawn.

In general our cases have been divided into two groups. In the first, 125 operations were performed for gross conduct disorders the majority being patients with long-standing psychoses. The second group of 54 were considered to have a possible chance of recovery by operation judging them as a whole, even though in all but four paranoid schizophrenics each had been treated by the usual methods such as insulin comas, convulsion therapy and prolonged narcosis.

Classifying the results into good, fair and poor, 9% of the 125 in the first group were good, 42% were fair and 46% were poor. Of the 54 in the second group, however, 37% were good, 37% fair and 22% poor.

TABLE I.

	Good	Fair	Poor	Died	Total cases
Group 1: Conduct ...	9%	42%	46%	3%	125
Group 2: Personality ...	37%	37%	22%	4%	54

An analysis of the cases according to the type of incision used is perhaps of greater interest from the point of view of this paper. In order to simplify the results and give adequate numbers for comparison the cases are divided into four groups representing seven types of bilateral incisions.

The first comprises those with an upper incision 6 cm. above the zygoma—the planes of section in these cases are probably variable. There were 15% good results in 52 cases. The catatonics did fairly well with this incision, 3 out of 9 making a good improvement.

The second group comprises those operated on by what we might call a middle incision. The leucotome was entered at a point 3 cm. above the zygoma and pointed at the junction of the middle and upper thirds of a line joining the zygoma to the vertex in the plane of the coronal suture on the opposite side of the skull. 11% of the 71 cases made a good improvement. 4 of the 8 good results in this group were paranoid schizophrenics.

The third section comprises three different incisions. The first was a bilateral horizontal cut by pointing the leucotome, from the temporal approach, at a point 1 cm. above the supra-orbital notch of the opposite side. The second incision was also horizontal but more posterior, the third combined the horizontal and middle vertical incisions. 20% of 30 cases in this series made a good improvement. 3 of the 6 good results were in paranoid schizophrenics but in each the vertical incision was also made. The other 2 making good improvements were agitated depressives with paranoid features who had not responded to full courses of convulsion therapy.

In the fourth group the material was better, being largely young schizophrenics who had failed to react to insulin and convulsion therapy. The two operations included in

Tables of leucotomy results are of such little value unless correlated with their previous prognosis that I would make a plea that whenever detailed tabular results are given a prognostic column should be included.

RELAPSES

Among these 48 cases there have been only 4 relapses. The 2 cases of agitated depression relapsed after approximately eighteen months, and 2 subjects of somatopsychic delusions after four to five months. The latter discharged themselves rather too early, and although one of them was free from symptoms at the time, neither had recovered. Variations both for better and worse often occur up to nine months or so after operation, but striking changes are uncommon after a year, and I think it is fair to say that patients who have kept really well for eighteen months may look upon themselves as permanently recovered.

A noteworthy feature of this series is the rarity of frontal lobe injury symptoms—notably emotional flattening, lack of initiative, indolence, irresponsibility, facetiousness and lack of modesty. These and other undesirable sequelæ have been an alarming feature of Freeman and Watts' series and must have great weight when considering leucotomy. Of the 26 patients in my series discharged from hospital or greatly improved only 1 showed any facetiousness and irresponsibility and only 3 any significant slowness and lack of initiative—and all 4 of these are earning their livings or looking after their homes. All my patients were operated on by Mr. Wylie McKissock and I wonder whether their relative freedom from frontal lobe symptoms may be due to some slight difference in his technique although I understand his methods are very similar to those of Watts. It is noteworthy that 3 of the 4 cases mentioned were operated on at the same session, although Mr. McKissock assures me that he did not consciously alter his technique on that occasion.

Lastly, it is of the utmost importance to discover in patients who have made good recoveries what brain changes are to be found. Dr. Alfred Meyer has demonstrated among other things varying degrees of degeneration of the dorsomedial nucleus of the thalamus, but none of his cases can be said to have fully recovered. It is not easy to obtain the brains of patients dying, perhaps years later, in the ordinary way of things. All we can do, and I think we ought to do, is to urge the nearest relatives of our patients to let us know if ever they are admitted to hospital, so that we can effect a liaison with their doctors.

Dr. R. Ström-Olsen: In Table I I have set out a summary of the results in 106 cases out of a total of 116 operated on at Runwell Hospital by Mr. Geoffrey Knight. From these results it will be seen that roughly two-thirds have benefited to a greater or lesser extent from the operation, whilst of the cases "not improved" 2 have actually been made worse mentally.

Indications for treatment are, of course, arrived at by a careful study and follow-up of cases treated. From this it would appear that the most favourable outcome can be expected in obsessional neurosis, chronic melancholia, whether involutional or otherwise, and in paraphrenia and chronic paranoid states showing psychomotor unrest and anti-social behaviour due to delusions and hallucinations. In the obsessional states successfully treated, all the patients completely lost their obsessive thoughts and compulsions and the results were really dramatic. In the other conditions mentioned the complete relief of emotional distress was also very apparent in the favourable cases. In other psychotic

TABLE I.—RESULTS IN 106 CASES.

Diagnosis	Social recovery	Much improved	Improved	Not improved	Deaths	Total
Melancholia (involutional and chronic)...	7	1	3	6	0	17
Paraphrenia	3	0	2	2	2	15
Schizophrenia	5	0	17	14	1	46
Epilepsy	1	2	2	2	1	11
Obsessional neurosis	4	1	2	1	1	9
Chronic mania	1	0	2	3	0	6
Psychopathic personality	1	0	0	1	0	2
Total	22	10	31	29	5	106

states, schizophrenia, epilepsy, chronic mania, psychopathic states, the effect was not quite so favourable although there were a number of social recoveries. The most important effect was that patients with a disturbing influence became quieter and more manageable, thus obviating the need for the same close nursing supervision as formerly, and the output and quality of these patients' work undoubtedly improved. There was no apparent effect on the incidence of fits in epileptics. The common factor in these conditions would appear to be the overwhelming effect of a severe and prolonged disordered emotion, and certain psychotic symptoms such as hallucinations and delusions, on the patient's

RESULTS

In giving the results of 48 patients treated at Bexley Hospital I am including only those operated on more than nine months ago, because the changes after leucotomy often continue for many months, and I do not think any reliable estimate of result can be made for at least nine months if not a year.

TABLE.

Diagnosis	Recovered or remitted	Greatly improved	Conduct improvement	No improvement	Died	Out of hospital	Known to be working	Relapsed	Total
Agitated depression	8	—	—	1	1	7	4	2	10
Schizophrenic reactions	2	1	1	1	—	3	3	—	5
Schizophrenia	5	4	7	5	1	8	7	—	22
Aggressive psychopaths, &c.	1	1	2	—	—	1	1	—	4
Other conditions	3	2	—	1	1	5	3	2	7
Total	19	8	10	8	3	24	18	4	48

By recovery I mean that the patient appears to be quite normal in conversation and conduct both to the physician and to relatives living with him; by remission, loss of all symptoms of the disorder for which he was treated. I have not attempted to separate these groups because the standard of normality is too equivocal. Several of those classed only as greatly improved are out of hospital doing full-time work or keeping house successfully.

Of the 10 agitated depressives, 7 had previously had E.C.T. with only temporary benefit; in the remaining 3 it was contra-indicated for physical reasons. 8 remitted and 6 remain quite free from symptoms; 2 relapsed to some extent. 1 died six days after operation and 1 shows no improvement.

Of those I have classified as schizophrenic reactions (admittedly a quite artificial group) the prognosis would have been promising had they not sounded a warning note by failing to respond to other treatments. Duration of symptoms averaged just under two years, but their extreme tension and distress associated with vivid hallucinations gave us little option but to operate. 2 have shown complete recovery for over two years and 1 other has been working for nearly three years.

In the schizophrenic group the prognosis was uniformly bad, and in a number of cases frankly hopeless and only conduct improvement to be expected. Nevertheless 3 of this group appear to have made complete recoveries and have stayed well during a period of three to four years, while 4 others are carrying on successfully at their jobs. One other has recently left hospital and I think will soon be earning her living. Only 5 have shown no improvement.

The prognosis in all 4 aggressive psychopaths was considered quite hopeless, yet one girl who had literally smashed up the hospital for nine years after her transfer from a mental deficiency colony in 1933 has become stable enough to earn her living in domestic work for eighteen months. One encephalitic has lost all her former all-too-frequent urges to smash and 2 others, a troublesome encephalitic and an aggressive epileptic, show some conduct improvement.

Other conditions include 3 subjects of long-standing somatopsychic delusions, one case of chronic mania, who remains materially unchanged, 2 mixed cases and 1 case of severe coprolalia and head striking (La Torette's syndrome). This lady whose symptoms dated back some eight or nine years and who had maintained for several years a completely bent-double position and was unable to complete a sentence without a half-dozen interpolations of the same obscene word, slowly but surely improved and is now at home living a normal life and is quite free from her habit-spasms. The somatopsychic delusional cases comprise a group difficult to classify, merging on the one hand with hypochondriacal depressives and on the other with paraphrenics, while all show a strongly obsessional attitude. The results were disappointing; one patient lost all his symptoms but failed to gain real insight and relapsed in four to five months, and another improved greatly but likewise relapsed; the third is in no way troubled by her delusions eight months after her leucotomy but they still remain in the background.

Dr. Freeman's remarks on the relief of pain through leucotomy are to some extent borne out in the case of a patient operated upon too recently for inclusion in my list. He described among other somatopsychic complaints, agonizing pain in the jaws and mouth. Since his leucotomy nearly three months ago he says this pain scarcely troubles him. He is, however, a chronic bronchitic subject to acute exacerbations and his somatopsychic complaints tend to wax and wane with his physical symptoms. It will be interesting to see whether his relative freedom from pain survives an acute attack of bronchitis.

It will be seen that out of 48 patients 24 are out of hospital and 18 known to be working full-time or looking after their homes. Considering the prognosis in these cases the results must be considered most encouraging, and in some of the schizophrenics they have been truly dramatic. I attribute the unusually good results in relation to prognosis to the fact that only patients showing marked tension were chosen and that leucotomy has not been performed as a routine on a mass of chronic hopeless psychotics.

often not noticeable during the patient's stay in hospital. An analysis of these undesirable symptoms is shown in Table III. It does not purport to be by any means a complete

TABLE III.—INCIDENCE OF UNDESIRABLE SYMPTOMS.
(Ascertained by Follow-up Visits to Relatives and Interviews with Patients at Clinics.)

	Cases
Selfishness, egocentricity, inconsiderate behaviour...	12
Deterioration of personal habits and manners ...	11
Aggressiveness... ..	9
Irritability	9
Lessening of affection... ..	8
Apathy, lethargy and lack of initiative	7
Volubility	6
Laziness	5
Emotional facility and childishness	5
Tactlessness	4
Bad language	4
Fatigue and excessive sleep	3
Loss of sense of responsibility	3
Impairment of sense of time	2
Incontinence of urine (occasional)	3

scientific analysis of the psychiatric complications and sequelæ. It is; however, a useful guide or statement of observations made by relatives, and shows the incidence of the various symptoms or complaints as observed by them, and/or the psychiatric social worker and psychiatrist. The true picture of the personality change can only be demonstrated by a detailed clinical history in each case. It is quite obvious, however, that there are many disquieting features in the changes observed.

Whilst there is no doubt that the balance of opinion is much in favour of the operation, one has to bear in mind the possibility of the development of these quite serious personality disorders before recommending any patient to undergo the operation. The following remarks made by relatives are illuminating: "She often embarrasses us but it is lovely to think she is so well", and "For her this operation has been a miracle, but we wish we had not got to live with her".

The *sine qua non* of indications are therefore (1) incurability by other means, (2) the severity and disabling effect of symptoms, and (3) chronicity.

One may speak with greater certainty and favour of the effect of leucotomy on selected patients of the chronic psychotic population of a mental hospital, i.e. paraphrenics, epileptics, schizophrenics, who are not likely to be discharged. In the majority of them, although leucotomy is only a palliative measure it has resulted in a marked improvement in the severe disturbance of behaviour seen in this type of case, and this improvement has been of great practical importance. Patients are quieter, more manageable, they feel more comfortable and require less nursing supervision than formerly, and their output and quality of work have improved.

Major J. N. P. Moore, R.A.M.C.: *Prefrontal leucotomy—Report on 150 cases at the Crichton Royal Hospital.*—When we considered using the operation more than three years ago we did so in a sceptical frame of mind, critical of the empirical nature of the procedure. For, while there is no doubt that the brain is the organ from which the symptoms originate, it is by no means certain that it is the seat of the disease process as a whole. Thus we chose cases, which, judged by ordinary prognostic standards, were hopeless, chronic invalids. Of the first 100 cases, a report on which was published six months ago, the average duration of the present attack was eight years and only 5 had been ill for less than two years. In most of them the better established forms of treatment such as electric convulsion therapy and insulin therapy had failed to produce more than transient improvement. The criterion for selection of cases was the presence in the clinical picture of signs of mental tension, shown by such symptoms as irritability, rage, fear or other forms of emotional excitation, insomnia, and on the motor side, restlessness, aggressiveness, destructiveness or impulsive behaviour.

Now the series has increased to 75 male and 75 female patients whose average age was 35 years, ranging from 18 to 65 years. It includes 8 cases of melancholia showing marked signs of tension for many years, a case of recurrent mania of ten years' standing, and 7 severe obsessional states. It also includes 4 organic cases; these are a general paretic who after fever treatment developed a chronic hallucinosis, a Parkinsonism with a super-added agitated depression, and 2 epileptics subject to fréquent equivalents with impulsive outbursts. The remaining 130 cases were suffering from schizophrenia—mainly aggressive, restless, negativistic paranoids and catatonics. Only 22 were hebephrenics. 8 of the catatonics showed a well-marked periodicity of their symptoms.

RESULTS

As pointed out in a previous communication, in chronic cases such as these it is not possible to adopt the rigid criteria of recovery that one would apply to more recent cases, and the grading of patients is thus to a certain extent relative to their pre-operative state. In order to make the meaning of the table quite clear I should like to define the standards

conduct, resulting in severe disability, anti-social behaviour, extreme restlessness, violence, destructiveness and suicidal tendencies. I purposely use the adjectives "severe" and "prolonged" because the present-day operation, even in the hands of the most expert surgeon, is fraught with dangers and risks which one cannot afford to overlook. I would therefore stress that cases should only be considered for leucotomy who have had a thorough trial of all other forms of treatment and whose illness has lasted sufficiently long to leave no reasonable doubt that a remission or recovery cannot take place by any other means, or where the disability is so extreme as to make the risk worth while. In our own series the duration of the illness in by far the majority of cases was more than five years. In only 9 was the duration under five years, and of these only 2 were between two and three years' duration.

In the 116 cases operated on the immediate post-operative deaths numbered 4, or 3.4%. All were due to cerebral hæmorrhage. Other deaths attributed to the leucotomy, occurring four and five months respectively after the operation, numbered 2. The cause in one case was toxæmia and exhaustion due to nutritional and trophic disturbances, and in the other, cerebral softening due to old hæmorrhage. Further, in 95 non-epileptic patients operated on, 6 developed epileptiform seizures, 3 of whom have been quite severely affected. I am not qualified to talk of the surgical aspect, but I would like to mention in passing that recent pathological evidence seems to show that hæmorrhage may be due to section of thin-walled veins, sometimes aberrant or anomalous in pattern, whose resistance cannot probably be felt even by the finest of instruments. This is obviously a grave drawback to the method of blind approach.

We are further hampered in framing criteria for indications by the fact that recent histological and other evidence tends to show that there is a very limited zone in the prefrontal white matter in which surgical section is effective in severing the all-important fibres, and that landmarks on the skull and surface of the brain would appear to be uncertain guides to this circumscribed zone.

Table II shows the analysis and follow-up of 31 cases discharged. Regarding the condition on discharge, 18 were observed in hospital for more than six months, 5 for three to six months and only 8 from one to three months. The duration since leucotomy in these

TABLE II.—ANALYSIS AND FOLLOW-UP OF 31 CASES DISCHARGED FROM HOSPITAL.

(1) Condition on Discharge :									
(a) Social recovery	17
(b) Much improved and improved	13
(c) Not improved	1
									31
(2) Deaths :									
Suicide	2
Natural causes	1
									3
(3) Readmitted to hospital (due to relapse or development of undesirable symptoms)									
	5
									5
(4) Employment :									
(a) Fully employed	11
(b) Part-time employment	9
(c) Not at any time employed	11
									31
(5) Condition at time of follow-up (March, 1946) :									
(a) Satisfactory result...	15 = 48.3%
(b) Partially satisfactory only, but definitely better than pre-operative state	9 = 29.1%
(c) Unsatisfactory result (including relapse or development of undesirable symptoms)	7 = 22.6%
									31
Total									31

cases varies from three months to four and a quarter years, the average duration being two and a quarter years. It will be seen, therefore, that out of a total of 31 cases discharged, nearly half, viz. 48.3%, have shown an entirely satisfactory result so far. In view of the very chronic and intractable nature of the cases treated, this number, although comparatively small compared with the whole series, must be considered highly gratifying. As the time which has elapsed since leucotomy is reasonably long there is every likelihood of these results being permanent, but of course the follow-up on all cases will continue and the condition will be reassessed from time to time. One significant observation is that while some patients can be regarded as recoveries or much improved whilst hospitalized and living under sheltered conditions, when they are discharged and have to adjust to outside life some break down and react unfavourably. From an intensive follow-up study in which both relatives and patients have been interviewed, either by our senior psychiatric social worker or by myself, it was apparent that the interaction of the patient with the outside environment brought out undesirable symptoms which were

our cases was the illness of shorter duration than three and a half years. 2 of our group of 8 melancholics recovered, 3 are much improved. Our one case of recurrent mania has had her operation too recently to judge the ultimate outcome but she has been consistently well during the ten weeks which have elapsed since her operation. Our experience with organic illnesses is too small to draw any conclusions but one of the two epileptics has improved in that her violent psychomotor equivalents are less severe, and the distressing agitation in the case of Parkinsonism has been relieved completely.

I may sum up by saying that the outstanding impressions gained from more than three years' experience of the operation are the excellent results in obsessional states, the encouraging results in chronic melancholia and above all, the remarkable change in outlook for the distressful cases of schizophrenia which form such a large proportion of the chronic population of our mental hospitals. The most urgent problem in regard to the operation appears to be the need for a systematic study of recovered cases, especially those who have had the treatment at an early stage of their illness in order to assess more accurately the degree of personality change which follows the lesion to the frontal lobes.

Dr. Jan Frank: *A review of 200 cases of leucotomy at Graylingwell Hospital, Chichester.*—The length of observation varies from eight months to three years. Social recoveries were regarded as those who are capable of independent management of their own affairs, occupy a post, have the type of work they had formerly, and are, at the same time, able to appreciate the enjoyments of life. Insight regarding their previous illness is not included in the definition of social recovery.

In the improved category are patients who attained a better social adaptability, are easier to manage, and have much fewer psychotic symptoms. They are not well enough to live on their own and are not self-supporting. More than half of the improved cases are for long spells, or permanently, in the care of their family. They are usefully occupied, though at times with stereotyped tasks. The average duration of hospitalization prior to the operation was four years, three months, ranging from a few months up to fourteen years. 35% of the total had spontaneous remissions lasting from three to eight months, but none got well enough to interrupt social invalidity, which in all was continuous and of at least three years' duration.

The indication for leucotomy in these 200 cases has been put forward as a last resort only. Other forms of treatment, including systematic psychotherapy when practicable, also outside the hospital, have been tried but failed. In the first 75 cases, distressing symptoms determined the choice of leucotomy. With more experience, our guiding criteria, apart from hopeless prognosis, were as follows:

A prepsychotic personality with good or fair record of social adjustment. In the clinical picture, a plasticity of symptoms such as delusional productivity, and some vestiges of resistance to total psychotic surrender should be present. Paramount of all is, however, a conflict situation with emotional colouring.

We found, from the psychiatric aspect, leucotomy contra-indicated in patients with *a priori* shallow affect, as revealed in the study of their prepsychotic personality. For schizophrenics in whom there is an established formal thought and language disorder (Kasanin, Goldstein), coupled with other primary symptoms, such as dissociation of conation, psychic anergy, the usefulness of leucotomy is problematical if the manifest psychosis is of longer than three years' duration. Nuclear schizophrenics of the chronic catatonic or paranoid group, if they do not respond to insulin, should have leucotomy as early as possible, before cognition is hopelessly disturbed.

Our observations and results bear out that in patients whose psychic drive is either constitutionally low, or slowly petering out, due to the schizophrenic process, a more anteriorly placed cut than that stipulated by Freeman and Watts should be performed. Mr. Ross, who operated on all the reported cases, takes his measurements on the skull 2½ cm. anterior to Freeman and Watts—when required to do so. With this modification we certainly achieved less spontaneity, loss of initiative and emotional bleaching, than in the first 75 cases which were all operated on according to Freeman and Watts' instructions.

Cerebral arteriosclerosis, organic senile syndrome, should be carefully excluded from the involutional group, as leucotomy precipitates their deterioration. If the clinical signs are ambiguous, the state of the retinal vessels, an "organic" Rorschach, and discrepancy of verbal to the disadvantage of performance intelligence test scores are of great value to us; also the positive correlation of high blood urea and organic mental condition, established by Richter. We found a blood urea of over 50 mg.% an absolute contra-indication for the operation. 16 patients in this series were over 55 years of age.

In paraphrenics, although the results are very encouraging, leucotomy is justified only when spontaneous improvement is excluded; in manic-depressives, although the classical Freeman and Watts posterior cut seems to be able to arrest the psychotic mood-swings, only too-quickly alternating episodes warrant leucotomy. The numbers are not sufficient to state with statistical validity whether leucotomy is definitely capable of stopping cyclothymic swings; the clinical impression, however, suggests that it does.

In assessing complications and results, it has been found impossible to state anything

we have adopted. The term "recovered" must be taken to mean social recovery, i.e. ability to leave hospital, live at home under normal conditions and resume some form of useful employment not necessarily up to former standard.

RESULTS IN 150 CASES.

	1943	1944	1945	1946	Total
Recovered... ..	8	19	16	—	43
Much improved	5	6	20	1	32
Improved	11	10	6	4	31
Slightly improved	12	5	11	3	31
Unchanged	2	5	2	—	9
Dead	4	—	—	—	4
Total	42	45	55	8	150
Discharged home... ..	10	23	23	—	56

43 patients can be regarded as recovered and they are all at present living at home; some of them have been well for as long as three years. All discharged patients have been followed up by personal interview or by correspondence with their relatives, family doctor, or with the patient himself.

32 patients come under the heading of "much improved" and 13 of them have been able to return to their families. In general this group includes patients who can now have parole, enjoy the amenities of the hospital and do useful work under supervision.

Altogether 56 patients of the "recovered" and "much improved" groups have been able to return home.

31 patients have "improved". Many were previously serious nursing problems and now take part in occupational and recreational therapy, or do simple work in the hospital or on the farm.

31 patients have "improved slightly" and this has usually meant the loss of certain troublesome features of their illness such as violent or impulsive behaviour, faulty habits or destructiveness; other symptoms persist.

9 patients may be regarded as "unchanged" and remain in approximately their pre-operative state.

These results are not final in many patients, since we can expect that our more recent cases will continue to improve. Periodical surveys of our case material indicate that improvement can continue for as long as three years after the operation. Similarly we appreciate that the possibility of relapse cannot yet be ruled out. Besides the evanescent post-operative improvement which sometimes occurs, some cases improved for a time and then relapsed—several, for example, went home for short periods. None of these was among our best cases and we have had no major relapses in patients who could be included in our "recovered" group. So far none of our surviving patients can be regarded as worse as a result of the operation. Our 4 fatalities occurred early in the series and we have had none among the last 120 cases.

DISCUSSION

These results are encouraging and the scepticism with which the operation was originally regarded in our hospital has given place to tempered enthusiasm for this new form of treatment in carefully selected cases. In achieving these results our experience has convinced us that re-education plays a major part in determining the quality of the remission. The conception that the injured cerebral tissues have their functions progressively taken over by other areas cannot be over-emphasized and should be the basis of our attitude towards re-education. Co-operation between medical officers, nurses, and occupational therapists is necessary and a scheme for the re-education of the individual patient should be arranged. I would go so far as to say that the operation should not be undertaken unless facilities exist for expert rehabilitation.

Our most considerable experience has been with schizophrenics and now we feel that the operation should be carried out in old-standing cases who fulfil the criteria I have outlined. It may be of interest to note in these cases we have found that a well-established periodicity of the symptoms is a favourable prognostic sign.

In earlier schizophrenics where tension is a prominent feature and where insulin and E.C.T. have been thoroughly tried one should not hesitate to consider the operation if clinical judgment indicates that the case is deteriorating and reasonable hope of a spontaneous remission can be ruled out. In our hospital the decision to operate is taken only after the case has been discussed fully at a meeting of the medical staff.

By far the best outcome was achieved in our small group of obsessional, 6 of our 7 cases have recovered, the seventh has improved and may yet recover. We feel therefore that a lifelong obsessional should have the benefit of the operation if psychotherapy has failed to relieve his condition and if his symptoms so grossly interfere with his existence that he cannot live an ordinary life. One has to be careful, of course, to exclude those cases where the obsessions are merely symptomatic of, or temporarily exaggerated by, an underlying endogenous depression. Our group of melancholics is small because the results of E.C.T. are favourable and only when patients relapse so frequently that they cannot live outside a mental hospital do we consider the operation advisable. In none of

our cases was the illness of shorter duration than three and a half years. 2 of our group of 8 melancholics recovered, 3 are much improved. Our one case of recurrent mania has had her operation too recently to judge the ultimate outcome but she has been consistently well during the ten weeks which have elapsed since her operation. Our experience with organic illnesses is too small to draw any conclusions but one of the two epileptics has improved in that her violent psychomotor equivalents are less severe, and the distressing agitation in the case of Parkinsonism has been relieved completely.

I may sum up by saying that the outstanding impressions gained from more than three years' experience of the operation are the excellent results in obsessional states, the encouraging results in chronic melancholia and above all, the remarkable change in outlook for the distressful cases of schizophrenia which form such a large proportion of the chronic population of our mental hospitals. The most urgent problem in regard to the operation appears to be the need for a systematic study of recovered cases, especially those who have had the treatment at an early stage of their illness in order to assess more accurately the degree of personality change which follows the lesion to the frontal lobes.

Dr. Jan Frank: *A review of 200 cases of leucotomy at Graylingwell Hospital, Chichester.*—The length of observation varies from eight months to three years. *Social recoveries* were regarded as those who are capable of independent management of their own affairs, occupy a post, have the type of work they had formerly, and are, at the same time, able to appreciate the enjoyments of life. Insight regarding their previous illness is not included in the definition of social recovery.

In the *improved* category are patients who attained a better social adaptability, are easier to manage, and have much fewer psychotic symptoms. They are not well enough to live on their own and are not self-supporting. More than half of the improved cases are for long spells, or permanently, in the care of their family. They are usefully occupied, though at times with stereotyped tasks. The average duration of hospitalization prior to the operation was four years, three months, ranging from a few months up to fourteen years. 35% of the total had spontaneous remissions lasting from three to eight months, but none got well enough to interrupt social invalidity, which in all was continuous and of at least three years' duration.

The indication for leucotomy in these 200 cases has been put forward as a last resort only. Other forms of treatment, including systematic psychotherapy when practicable, also outside the hospital, have been tried but failed. In the first 75 cases, distressing symptoms determined the choice of leucotomy. With more experience, our guiding criteria, apart from hopeless prognosis, were as follows:

A prepsychotic personality with good or fair record of social adjustment. In the clinical picture, a plasticity of symptoms such as delusional productivity, and some vestiges of resistance to total psychotic surrender should be present. Paramount of all is, however, a conflict situation with emotional colouring.

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definite before at least six months have elapsed after the operation. The mental state within this period, however stormy, or startlingly free from psychotic symptoms, has no relevance for the final outcome. The same applies to neurologic complications, organic confusional states, incontinence, perseveration. All these were more frequent by the posterior cut—only one, however, remained permanent. One patient developed an extrapyramidal permanent neurologic complication. Since operation, he has choreiform jerks resembling those of Huntington's chorea. (His mother died of some form of chorea.) He was refractory to the operation and is still an unrelieved paranoid schizophrenic. 15% of our cases had urinary incontinence which lasted more than two months, but in none did it remain a persistent disability.

18 patients had major epileptiform convulsions, usually one or two; 2 cases had six fits at short intervals. Although the E.E.G., according to Dr. Hill's personal communication, is normal three months after the operation, the great majority of our 18 cases first had fits six months after. 15 had posterior, 3 anterior cuts. After two to four months' anti-convulsive drug administration, no recurrence of convulsions was observed later than eight months after the operation.

A slight flabbiness of the innervation of the facial muscle—rendering the mimical expression less distinct than before—is in few a lasting sequelæ, although in many cases it is very marked during the days immediately after the operation. Bulimia is a relatively frequent post-leucotomy symptom in our patients, but disappears in from six to twelve months after. The ravenous appetite may also be responsible for some unusually rapid gains in weight. Some of our females showed hirsutic changes (7 patients), 4 of them previously had a pronounced facial growth of hair, but after leucotomy they developed a veritable beard. Nothing definite emerged concerning their menstrual cycle; some reported amenorrhœa following the operation.

Intelligence.—96 were tested. The impairment of simultaneous grasp, and of discriminative conceptual thinking, which we observed by psychometric testing, and from reports from the patients themselves, and the tendency to perseveration were not noticeable any more after the follow-up of ten months. In fact, apart from the age-group over 55, we could not detect any impairment of cognition or any intellectual deficit after the lapse of one year. We tested 96 cases with the Herring, Modified Stanford Binet, Raven's Matrices, Kohs' Blocks, Pass-along Tests, but could find no significant difference in their general intelligence, except that in the recovered cases their scores showed less scatter. Patients over 55 display a discrepancy of their vocabulary, verbal and performance scores—in some consisting of a difference of 15 (I.Q.) points to the disadvantage of performance; 10 out of 16 patients. We tested these cases also with Rorschach; we could not surmount, however, the difficulty of familiarity with the blots when shown before and after operation, so we found it impossible to utilize these in our findings with regard to post-operative personality changes.

None of the patients regained true insight in the full sense of the word, or is able really to appreciate what the operation was for, or its importance. The direct effects of the operation on psychic life are those on the personality. The specific change which was verified in the surveyed cases was a poverty, or entire lack of dreams, and a thinning, or disappearance of dereistic experience—they cannot daydream about their wishes, or be abstractly angry in a sustained fashion. They become, due to this emotional asymbolia, more plain, matter-of-fact like. In many ways it has a resemblance to slight senile personality changes. Owing to the emotional desensitization, the passions and conflicts which are expressed in their psychosis gradually shift out of focus: very similar to old men who can look serenely upon the follies of their youth. Similarly also, to senile personality changes, post-leucotomy patients do not like adventure, but want to remain in a more or less stereotyped routine of activities. The learning ability for new knowledge is, as some complain, reduced. In the old involuntal melancholic the paradox occurs that the desperate loneliness of oncoming senility is alleviated by reaching faster the state of a happy dotage. This is borne out, not only in the personality changes, but in the neurologic symptoms also: e.g. if they have had a tremor of the hands it gets worse after leucotomy. Their gait, too, becomes less steady.

We had no patient in this series who was worse after the operation. Whether the 3 improved cases who, more than a year after, still manifest frontal disinhibition and are unrestrained, selfish, family tyrants, are due to more extensively damaged frontal areas owing to anomalous placing of the cut, or some secondary changes, is impossible to say. The topographical variability of the incision, decisively proved by A. Meyer, is unavoidable with the present technique, and a grave drawback. In our series there was no clinical disadvantage accruing from the more anterior incision—but certainly much less spontaneity and loss of initiative—which is quite frequently observed in the posterior, more extensive cut.

Mortality.—We lost 5 patients directly attributable to leucotomy. 4 died of cerebral hæmorrhage, 1 of staphylococcal meningitis. The percentage is 2.5%. 3 died of intercurrent illness more than a year after the operation.

Relapses.—2 paraphrenics classified as recovered, relapsed; both after a year—one as a result of harassing environmental circumstances. 1 schizophrenic classified as improved relapsed after three months; an improved aggressive psychopath relapsed eight months after the operation.

SUMMARY

The clinical results of prefrontal leucotomy in 200 cases of chronic mental illness have been reported. The time of follow-up was seven months to three years. Out of 92 schizophrenics, 19 (20.7%) socially recovered; 28 (30.4%) improved; 45 (48.9%) remained unchanged. In certain types of schizophrenics, caution is expressed with regard to the

LEUCOTOMY.—ANALYSIS OF THE RESULTS OF THE FIRST 200 CASES. (GRAYLINGWELL HOSPITAL.)

	M.	F.	Total	M.	Social recovery		M.	Improved		M.	Not improved		Died
					F.	T.		F.	T.		F.	T.	
						%			%			%	
<i>Schizophrenic group—</i>													
Catatonic	8	7	15	1	2	3	1	2	3	6	3	9	—
Hebephrenic	8	2	10	—	—	—	2	—	2	6	2	8	—
Simplex	18	9	27	1	2	3	10	1	11	7	6	13	—
Paranoid	20	20	40	7	6	13	6	6	12	6	8	14	1 (M)
With formal thought disorder ..			64			6			25			33	—
Without formal thought disorder ..			28			13			3			12	—
Schizophrenic total	54	38	92	9	10	19	19	9	28	25	19	44	—
<i>Paraphrenic group—</i>													
Paraphrenia	15	23	38	7	15	22	6	5	11	2	3	5	—
Paranoia	3	—	3	3	—	3	—	—	—	—	—	—	—
Paraphrenic total	18	23	41	10	15	25	6	5	11	2	3	5	—
<i>Affective disorders—</i>													
Cyclothymia	6	10	16	5	7	12	—	2	2	1	0	1	1 (F)
Involutional depression	13	23	36	10	14	24	3	5	8	—	1	1	3 (F)
Affective total	19	33	52	15	21	36	3	7	10	1	1	2	4
<i>Aggressive and oligophrenic psychopathies</i>													
Aggressive and oligophrenic psychopathies	6	5	11	1	—	1	4	3	7	1	2	3	—
Chronic obsessional neurosis	3	1	4	2	1	3	1	—	1	—	—	—	—
Grand total	100	100	200	37	47	84	33	24	57	29	25	54	5 (M, 1) (F, 4)
						42			28.5			29.5	

Section of Ophthalmology

President—P. E. H. ADAMS, F.R.C.S.

[February 14, 1946]

Lesion of Left Macula.—VIOLET M. ATTENBOROUGH, D.O.M.S., for E. F. KING, F.R.C.S. Male, aged 52. Caretaker. First seen at Moorfields in February 1943. He complained of gradual loss of vision in the left eye. His right vision was then 6/6 and his left vision was 6/18. On examination he was found to have some fine pigmentary disturbance at his left macula.

In June 1943 his left vision had improved to 6/12. May 1944, his left vision had fallen to less than 6/60.

On examination.—There was a raised mass on the temporal side of the left macula and some pigmentary disturbance and oedema at the macula itself. About this time he was shown at one of the Society's meetings.

Since then he has been kept under observation and a series of drawings have been made. There are now hæmorrhages present below the sub-retinal mass. His vision is now: Right (with glasses) 6/6 and left (with glasses) less than 6/60.

Investigations.—W.R. negative. Report from E.N.T. Hospital negative. Urine normal. Blood-pressure 150/95.

Mr. J. H. Duggart said that in his view this was certainly inflammatory. It was a low-grade bilateral chorioïdo-retinitis central and peripheral. There were multiple small foci all round the periphery, definitely more than stippling within normal limits. There were also early changes around the macula consisting of ill-defined overlapping yellow dots. He had watched for some years cases like this, in which, in the earlier examinations, one eye was not involved but became involved after two or three years. He thought that this condition was inflammatory and that the prognosis was bad.

Mr. E. F. King said that he took a different view from Mr. Duggart. In his opinion the changes were degenerative, not inflammatory.

Mr. Eugene Wolff thought that this was a case of disciform degeneration of the macula most probably due to hæmorrhage from the choriocapillaris. The patient was rather younger (52) than the classical type but he did not think that mattered.

The President said that if the case was ten or fifteen years older there would be no doubt that it was a vascular degenerative condition, but some people did degenerate earlier, and he thought that this might be one of those cases.

Tuberculosis of the Conjunctiva.—E. F. KING, F.R.C.S.

Girl, aged 14 years. Bacteriological examination had shown a large number of tubercle bacilli in the conjunctival ulcer in the left upper fornix. Opinion was evenly divided as to whether an attempt should be made to do anything surgically—local removal of the ulcer—or whether reliance should be placed only on sanatorium treatment. Calciferol had been suggested.

The lungs were normal and there were apparently no other tuberculous foci in the body.

Mr. C. B. Goulden said that in cases of tuberculosis of the conjunctiva the lesion should be removed if it were not too big and if not too much conjunctiva had to be sacrificed. Otherwise he would suggest general radiation with ultraviolet light, and tuberculin. Mr. S. H. Browning, who had had a large experience of these cases, said that that had been the plan he had followed. In the speaker's view, in this case, the lesion was too big to be dissected away; it would involve too much sacrifice of conjunctiva.

Mr. Affleck Greaves agreed that excision would involve too much sacrifice of conjunctiva. He suggested that a course of treatment with calciferol might be tried in view of the successes obtained with this drug in lupus cases. Also local treatment with ultraviolet rays by means of a quartz applicator might be beneficial, care being taken to protect the eye with a contact shield.

Mr. Frank Juler had seen this case at hospital and he was in favour of excising the ulcerated area, as it seemed to him that nearly all of it could be got away. With a primary tuberculous lesion as complete removal as possible should be the better procedure. His feeling was in favour of excision, to be followed by radiation of the regional glandular enlargement, and general treatment on sanatorial lines.

Mr. P. M. Moffatt had seen a similar case just before the war. It was decided to send the patient away to a sanatorium, and when he came back he was, as far as could be ascertained, perfectly cured.

A member said that he would strongly suggest tuberculin treatment.

Mr. King thought the essential lesion was very localized and the follicular reaction secondary.

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indication of operation. The importance is stressed of painstaking personality studies and also of clinical differentiation. The affective disorders and paraphrenics responded best to the operation. From 16 cyclothymics, 12 (75%) socially recovered. From 36 involuntional melancholics, 24 (66·7%) recovered. Among 38 paraphrenics, 22 (57·9%) socially recovered. A small number of chronic obsessional neurotics underwent the operation: 3 out of 4 recovered. In 11 mostly oligophrenic aggressive psychopathies operated on, the results were disappointing: 1 socially recovered, 7 were somewhat improved, the rest remained unchanged. No cases were considered worse. It is assumed that the emotional asymbolia observed after leucotomy determines mainly the personality changes which have the curative effect in chronic mental illness. The general intelligence is not affected by the operation in patients less than 55 years of age. The mortality rate was 2·5% (4 of cerebral hæmorrhage, 1 of staphylococcal meningitis).

My thanks are due to Dr. J. Carsc, Medical Superintendent.

Dr. William Sargent (*Sutton Emergency Hospital*) discussed a series of over 20 cases of intractable neurosis and psychosis which had had this operation without being admitted to a mental hospital. Obsessional symptoms, rumination and tension were generally relieved to a variable extent. Some cases had been able to return home in as little as a fortnight after the operation while others needed skilled rehabilitation in a neurosis centre. The operation should be extended beyond the confines of a mental hospital atmosphere and the chronic type of mental hospital patient. But psychiatrists had to be certain from a first-hand working knowledge of all other treatments, both physical and psychological, that these had been properly used or were unlikely to succeed.

Referring to Professor Freeman's use of leucotomy for the relief of unbearable pain, he wished to report what might well be the first case in which a modified leucotomy had been used in a case of intractable dermatitis, resistant to all previous treatments for many years. The patient was obsessed with her condition and the more she worried the more she scratched. She had previously been in a mental hospital for short periods because of her agitation, and was thought a suicidal risk at the time of operation because of her persistent suffering. As a result of the operation she lost her tension and scratching. Her dermatitis subsided. With minor ups and downs this remarkable improvement had been maintained for over two years. Only a modified operation was done and no obvious mental deterioration was observed. She still kept house and led an active life. It might be necessary to do a more thorough operation on similar cases in the future because recently this patient's obsessional anxiety was returning with increased skin irritation and scratching. This was probably due to gradual reformation of basic personality patterns described by Professor Golla. In two cases of obsessional neurosis, a second operation had been more successful where a limited first operation had resulted in improvement with a return of symptoms.

Dr. U. M. Hickman, whilst fully agreeing that prefrontal leucotomy should not be performed until full courses of insulin and E.C.T. had been tried, felt that leucotomy should not become an operation primarily to be carried out in general rather than mental hospitals.

At Warlingham, where they had performed just under 100 leucotomies, all but three had both insulin and E.C.T. and in most cases combined treatment. The three exceptions were contra-indicated by physical illness, pulmonary tuberculosis in two cases, spinal caries in the other case.

After the operation much care and thought were spent on the rehabilitation of the patient, adapting the routine to suit each individual case. They had found that suitable occupational and recreational therapy played an important part in the re-socialization of these patients, and one of the most useful methods of employment, in suitable patients, was to allow them to work in the patients' canteen and club—this provided social contacts and developed a sense of responsibility. Dr. Moore had already stressed the importance of rehabilitating the post-leucotomy patient. Surely the whole sequence of pre-operative treatment, the insulin, E.C.T., &c., the operation and the rehabilitation should be carried out by the same medical officers and nursing staffs, if a proper assessment of the patient's responses and degree of return to normality were to be observed, and this was only possible in a mental hospital.

Dr. Isabel Wilson suggested that photographs before and after leucotomy might be taken with similar lighting, dress and background, and that clinical notes after should if possible be comparable with those before, and not be confined to fresh aspects of the case.

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Since then he has been kept under observation and a series of drawings have been made. There are now hæmorrhages present below the sub-retinal mass. His vision is now: Right (with glasses) 6/6 and left (with glasses) less than 6/60.

Investigations.—W.R. negative. Report from E.N.T. Hospital negative. Urine normal. Blood-pressure 150/95.

Mr. J. H. Doggart said that in his view this was certainly inflammatory. It was a low-grade bilateral choroido-retinitis central and peripheral. There were multiple small foci all round the periphery, definitely more than stippling within normal limits. There were also early changes around the macula consisting of ill-defined overlapping yellow dots. He had watched for some years cases like this, in which, in the earlier examinations, one eye was not involved but became involved after two or three years. He thought that this condition was inflammatory and that the prognosis was bad.

Mr. E. F. King said that he took a different view from Mr. Doggart. In his opinion the changes were degenerative, not inflammatory.

Mr. Eugene Wolff thought that this was a case of disciform degeneration of the macula most probably due to hæmorrhage from the choriocapillaris. The patient was rather younger (52) than the classical type but he did not think that mattered.

The President said that if the case was ten or fifteen years older there would be no doubt that it was a vascular degenerative condition, but some people did degenerate earlier, and he thought that this might be one of those cases.

Tuberculosis of the Conjunctiva.—E. F. KING, F.R.C.S.

Girl, aged 14 years. Bacteriological examination had shown a large number of tubercle bacilli in the conjunctival ulcer in the left upper fornix. Opinion was evenly divided as to whether an attempt should be made to do anything surgically—local removal of the ulcer—or whether reliance should be placed only on sanatorium treatment. Calciferol had been suggested.

The lungs were normal and there were apparently no other tuberculous foci in the body.

Mr. C. B. Goulden said that in cases of tuberculosis of the conjunctiva the lesion should be removed if it were not too big and if not too much conjunctiva had to be sacrificed. Otherwise he would suggest general radiation with ultraviolet light, and tuberculin. Mr. S. H. Browning, who had had a large experience of these cases, said that that had been the plan he had followed. In the speaker's view, in this case, the lesion was too big to be dissected away; it would involve too much sacrifice of conjunctiva.

Mr. Affleck Greeves agreed that excision would involve too much sacrifice of conjunctiva. He suggested that a course of treatment with calciferol might be tried in view of the successes obtained with this drug in lupus cases. Also local treatment with ultraviolet rays by means of a quartz applicator might be beneficial, care being taken to protect the eye with a contact shield.

Mr. Frank Juler had seen this case at hospital and he was in favour of excising the ulcerated area, as it seemed to him that nearly all of it could be got away. With a primary tuberculous lesion as complete removal as possible should be the better procedure. His feeling was in favour of excision, to be followed by radiation of the regional glandular enlargement, and general treatment on sanatorial lines.

Mr. P. M. Moffatt had seen a similar case just before the war. It was decided to send the patient away to a sanatorium, and when he came back he was, as far as could be ascertained, perfectly cured.

A member said that he would strongly suggest tuberculin treatment.

Mr. King thought the essential lesion was very localized and the follicular reaction secondary.

JUNE—OPHTH. 1

DISCUSSION: INDICATIONS FOR THE TECHNIQUE OF INTRACAPSULAR EXTRACTION OF CATARACT

Dr. O. M. Duthie (Manchester): Opinions on the advisability of intracapsular extraction still appear to be divided. I think, however that whatever the merits or demerits of extra- or intra-capsular operation may be, it is right that any surgeon should choose that type of operation which suits him and his fingers best and in which he feels he can produce the best results for his patients.

Because of this, for the last eleven years I have practised only Sinclair's method of intracapsular extraction by tumbling. Sinclair's technique can certainly be mastered by any surgeon of reasonable ability, though judgment of its value can only be based on the end-results of the operative and post-operative complications as contrasted with other methods. Apart from a few exceptions, with which I shall deal later, this operation can be performed on all types of cataract.

It is a matter of great regret that no textbook and no article of importance fails to stress the difficulty of the operation in the hands of the young surgeon (or, for that matter, any other surgeon)—this is untrue and puts every young man off before he starts. Far better would it be to let him commence with the idea that nothing unusual is required except a great attention to detail and this should apply equally to every eye operation. I am here concerned only with two aspects of the problem—the method and the indications.

Dr. Duthie went on to discuss, with the aid of diagrams, the details of the technique of Sinclair's tumbling method, emphasizing the details of local anaesthesia, lid sutures, full iridectomy, puncture of an intumescent lens, the correct rocking movements after grasping the capsule, counter pressure from below after dislocation, and final toilet. The technique was further illustrated by means of a coloured cinematograph film.

Finally, the indications were discussed at length, the opener emphasizing his view that all types of cataract, over the age of 30, and unless general conditions contra-indicated operation, were suitable for intracapsular extraction. Particularly did this apply to high myopes, diabetic and secondary cataracts and immature cataracts of all types.

Loss of vitreous was discussed in full and finally, an analysis was given of 1,000 consecutive intracapsular extractions, with their end-results and surgical complications.

Mr. John Foster (Leeds): As my instructors invariably employed the extracapsular technique, I followed suit in independent practice from 1912-1937.

By then, personal observation of intracapsular extraction with forceps in Continental clinics had convinced me that the dangers of the method had been exaggerated. Later observation in Edinburgh confirmed this. Since July 1937 I have performed or helped my assistants perform about six hundred intracapsular extractions. Naturally, at first vitreous and iris prolapse and the ruptured capsule presented greater problems than with the extracapsular method. I tried expedients advised by various intracapsular operators to counter them, retaining those which were effective.

The technique finally adopted has been static too short a time to offer statistical proof; nevertheless, as these procedures have so greatly improved my control over difficulties, I feel that they may be of interest to anyone thinking of changing to the intracapsular method.

There are certain minor difficulties which are severally negligible, but collectively upsetting to patient or surgeon. As Cruise has taught, both should be "surgically comfortable" for a good result.

Simplification of technique and instruments may ensure this in a day of rapidly changing subordinate staff. I avoid mentioning knives in this connexion, as this subject requires a complete lecture to itself.

Pre-operative period.—Patients are upset by too much treatment before and after operation, and I would omit even the most traditional procedures unless they have an experimental or controlled clinical basis.

I would agree in stigmatizing dentiveses (Evans, 1939), hæmostatics (de Voe, 1942) and routine dental treatment (Wright, 1937) as useless, and have not employed them for ten years. I except a transfusion for pernicious anaemia, and a few days' pre-operative rest in the ward (if quiet) for very high blood-pressure.

I have admittedly not tried pre-operative phlebotomy as a preventative of expulsive hæmorrhage, as although highly regarded in Europe, its effect on the blood-pressure is only transient (Miller, 1926). For several years I have disregarded pre-operative

cultures (Foster, 1941), although they are taken in the routine manner (Mayweg, 1911; Schönemann, 1911; Lindner, 1915). As will be noted from Table I my infection rate (Clinic A) is lower than that of my colleague (Clinic B) in the same hospital, who operates on "clean" cases only. Of my own infected cases four were "clean" and of the four "dirty" ones two had infected lacrimal sacs that routine syringing (later instituted) would have detected.

TABLE I.

		Number	"Dirty" culture	Post-operative infection	%
Clinic A	...	358	22	8	2.21
Clinic B	...	200	—	5	2.5

That the weakness of the culture, up till now, as an indicator of post-operative infection is probably in part due to misconception of the relative pathogenicity of organisms and in part due to the inefficacy of antiseptics subsequently used, is shown by the results of Dunnington and Khorazo (1945) who found that the 11 infected cases occurring among 2,504 operations did not arise from pneumo- or strepto-cocci, but all occurred among 529 cases containing a particular *S. aureus*. Subsequently, by the use of antibiotics in such cases, they obtained the striking result of 663 cases with no infection, as compared with 730 cases treated by a conventional antiseptic in which 13 became infected.

The theatre.—Among the minor troubles of the theatre is the face mask. For so short a working distance it is essential to cover the operator's nose (I. Walker, 1930, and J. S. Davis, 1934) and unless it is short enough in front and provided with a chinpiece to keep it half an inch below the orbital margin, it is liable to rise above and obstruct the view [pictures shown]. An iron wire fitting close to the bridge of the nose is also useful to prevent "steaming", if the mask has the modern cellophane insert (Blatt and Dale, 1930) and the operator wears glasses.

Unless the operator wears gloves, long sleeves on the gown are a nuisance, best overcome by attachment of an orthopaedic stockinet cuff. One cannot always get short sleeved gowns in a general hospital.

Preparation of the patient: Soaping the eyelids in the theatre is waste of time; it takes three minutes "scrubbing" (literally) to remove the "transient" and two and a half hours' scrubbing to remove the "resident" flora of the skin (Price, 1938a; Durward, 1945).

Washing is best done by the patient in the conventional manner in the ward (Price, 1938b). 2% cetavlon which is virtually non-irritant is a better antiseptic than iodine round the eye, and being a "cationic soap" would permit of "washing" in a grossly dirty patient.

I doubt if irrigation does more than remove dirt mechanically, and have used normal saline for this purpose in the theatre for years.

The spouts of undines frequently break during repeated sterilization, and the lotion is difficult to keep at body temperature during a long list.

The American thermostatically controlled solution cupboard holding a number of filled, sterile undines is the best answer to this problem. My attempt to construct one here during the war failed, as I could not get adequate thermostats, or heating elements to give convection with a smooth, sterilizable surface.

The sterile towels to cover the patient's face are as a rule inadequate (allowing sutures to trail on the skin), complex, or requiring a clip. In Scandinavia and in Prague (Elschnig, 1922) a simple perforated towel with a selvaged opening avoids these difficulties. The mesh must be fairly open to allow the patient to breathe through it, and the opening at least 6 by 5 cm. to allow about 1 cm. shrinkage to the size of the orbit (5 by 4 cm.) (Richet and Luschka, 1922) with use.

The temperature of most ophthalmic theatres is too high as a rule for operations performed under local anaesthesia; a swing door to the sterilizing room may control this.

The lighting of cataract operations is a major problem. The fewer the people round the table the better, and the somewhat shaky nurse to whom the Hammer lamp is delegated is not a valuable addition.

Failure to use a new bulb, or to obtain correct centring (by an even chromatic edge to the disc of light) may reduce the already moderate illumination of a Lister lamp to a lower level. Table II gives the (makers') comparative figures showing the superiority of the scialytic lamp in this respect.

TABLE II.

		Dist.	Circle	Fixation	Intensity—f.c.
Lister	...	34 cm.	9 cm.	Shaky	86-148 (centring effect)
Scialytic (36 in.)	...	117 cm.	25 cm.	Firm	600 (75 in shadow of the hand)
Scialytic (18 in.)	...	105 cm.	25 cm.	Firm	1,000 (300 in penumbra of focus)

The makers' figures are given here, as my own observations with a photometer on lamps in use for some time gave lower figures. By holding the Lister lamp more closely (as can be done in capsulotomy) the illumination can be raised above 500 f.c. and avoidance of the reflex has certain advantages. So short a working distance is obstructive during lens extraction.

Syringes.—Some makes of syringe leak at the junction of syringe and needle mount, unless held together by two hands. This means that the forceps holding the tissue fold for injection have to be held by an assistant.

The "Luer-Lok" syringe prevents this leakage, and ensures one-handed use. Backward leakage may occur from rusting of the needle bore (much reduced by drying after use with the pneumatic needle dryer of Brunett and Flagg), or dissolution of a glass piston by alkaline boiling. This last requires a new syringe, as leakage deprives one of all idea of the volume of fluid injected behind the eye.

I have been unable to obtain a $1\frac{1}{2}$ in. "Luer-Lok" (American) needle in less than 23 gauge (rather too coarse for retrobulbar use) during the war, and as the exchange difficulty may persist it is interesting to know that a 26 gauge by $1\frac{1}{2}$ in. needle can be fixed in the original hub.

When a needle fails to perforate the skin, this may be due to a leathery skin, or to a needle defect. As the bore rusts before the exterior, if the needle is patent it is almost invariably due to a bent point. This is best detected by running the back and front of the point lightly over the finger-tip when the hook-like point catches in the papillæ. Such needles are most traumatizing. It should be noted, however, in these days of shortages, that they can be reclaimed later by pushing obliquely through a cork and rubbing on an Arkansas oil-stone.

The operation: Difficulties of access and vitreous loss.—I have not found vitreous loss to be the bugbear claimed with this method. I believe the method of access closely related to it. No speculum will fit all eyes adequately. The exposure I have found most helpful where the eye is not strongly upturned after retrobulbar injection, is the Gomez-Marques' (1940) superior rectus suture used without a speculum and with one or two retraction sutures in the lower lid. There is adequate access in spite of the slight "tenting" of the upper lid. If the superior rectus is very active, the suture is removed, and a big canthotomy and traction on the upper lid suture precede the section.

Capsular difficulties.—The frequency of taut, ungraspable capsules is reduced by the manoeuvre of Kirby (1936, 1941) (fig. 1). Pressure below the limbus at 4, 6, and 8 o'clock with the point of the lens expressor inwards for 2 mm. ruptures the zonule and renders the lower part of the capsule slack, and more easily grasped by subsequently applied forceps.

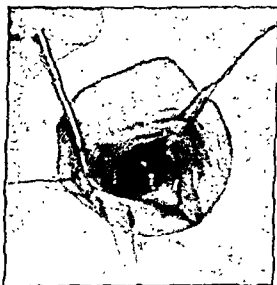


FIG. 1

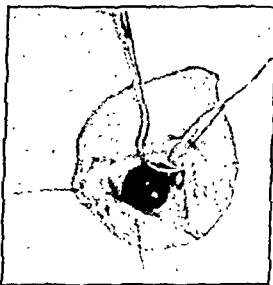


FIG. 2.

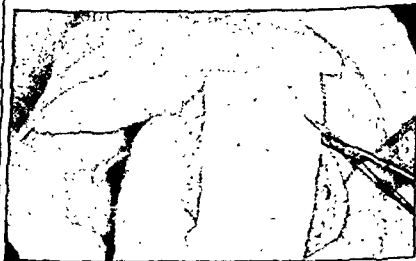


FIG. 3.

Where this fails the manoeuvre invented experimentally by Csillag (1936), used clinically by Traquair in 1941, and described in detail by the previous speaker, is employed.

Iris prolapse.—If prolapse of the iris recurs after reposition, as there is no danger of incarceration of the capsule, a complete iridectomy is justifiable.

Sometimes, however, this can be avoided by inserting a drop of 1% sterile eserine sulphate, and compressing the section as shown (fig. 2) with a lens expressor for a minute until the pupil contracts strongly. A peripheral iridectomy is then adequate.

Bandaging.—The safest, most rapidly applied and removed dressing of which I am aware, is Gluck's shield, held by two strips of elastoplast. I have used it without and with a minimum of dressing, so that all pressure is taken on the nose, brow, and cheekbone. A dressing which raises the shield from the bony prominences transmits any pressure on the shield to the eye and not to the facial bones.

A slight elevation of the shield permits division of the elastoplast which is left attached to the face and shortens the time of "dressing" enormously (fig. 3).

Convalescence.—Some relaxation of the traditional confinement to bed is due here. If at the first dressing (forty-eight hours) there is no evidence of prolapse or hyphæma, I allow my patients to get up. Mental disturbance and chest trouble are now much less frequent.

There are two obstructions to this policy. Few English hospitals have an adequate day room attached to the ward, nor have they adequate accommodation for patient's clothes, which are liable to be stolen.

As the pupil is clear and the eye free from inflammation in most cases, it is possible to refract them before discharge. Hamblin's "temporary cataract trial frame" glazed with a "flat" cylinder to which the appropriate plano-sphere for distance or reading can be clipped, allows the patient to use the eye at once, and has accustomed him to peripheral distortion by the time the refraction is stable. I have had several patients who preferred this form of frame to the conventional type.

On discharge the patient and his doctor seek information on his conduct during the next few weeks. The following instruction sheet which can be modified by erasion for an intra-ocular operation, saves a great deal of questioning and correspondence, if given to the doctor, and the relatives, a few days prior to leaving hospital.

Date.....

INSTRUCTIONS FOR M.....
FOR TREATMENT OF THE EYES AFTER OPERATION.

- (1) The edge of the eyelids are to be bathed every morning with a little piece of cotton-wool dipped in warm boracic lotion, to remove the discharge.
- (2) 1% atropine ointment should be inserted into the operated eye every morning after bathing.
- (3)should be inserted into the unoperated eye every morning after bathing.
- (4) No reading, bending, or walking about alone should be attempted, for fear of causing a hæmorrhage into the eye.
- (5) The metal shield (dark glasses) should be worn at night and during the day.
- (6) Walks out of doors if accompanied, or a ride in a motor car, are permitted, so long as the weather is fine.
- (7) The next appointment is for

In conclusion, may I say I am increasingly impressed with the rapid convalescence of the intracapsular as compared with the extracapsular extraction.

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Mr. F. A. Williamson-Noble said that Mr. Duthie had omitted to describe his useful manoeuvre of retracting the upper lid with a squint hook at the time of extracting the lens. In cases of cataract secondary to iritis with posterior synechiæ, did he just trust to wobbling the lens from side to side to free the adhesions, or did he separate them first with an iris repositor? The anonymous cataract glasses which Mr. Foster had described were, he thought, invented by himself; he had suggested the idea to Hamblin's a few years ago, and they had been making them for some time now.

Mr. M. Klein showed two drawings illustrating dissection with due regard to the position of the facial nerve.

The correct point for the injection, when the middle portion of the facial nerve is used for palpebral akinesia (O'Brien's method), lies at the junction of the middle and upper third of the distance between zygomatic arch and angle of the mandible on the condylar process.

Mr. M. D. Thakore asked whether the procedure described was the right one in a nervous patient, who was rather less helpful than others. Was it always essential that there should be a conjunctival suture? For over fifteen years he (the speaker) had used coagulen (Ciba) instead.

The makers' figures are given here, as my own observations with a photometer on lamps in use for some time gave lower figures. By holding the Lister lamp more closely (as can be done in capsulotomy) the illumination can be raised above 500 f.c. and avoidance of the reflex has certain advantages. So short a working distance is obstructive during lens extraction.

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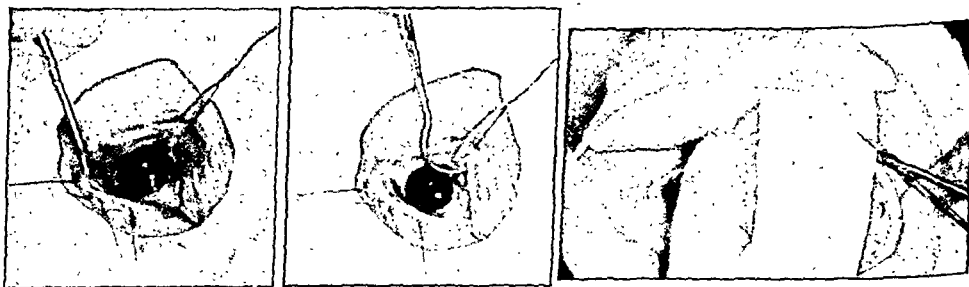


FIG. 1

FIG. 2.

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Section of Experimental Medicine and Therapeutics

President—E. N. ALLOTT, F.R.C.P.

[February 12, 1946]

DISCUSSION ON PENICILLIN IN THE TREATMENT OF SYPHILIS

Dr. James Marshall (*lately Adviser in Venereology to the War Office*): Until 1943, when it was demonstrated that penicillin possessed spirochaetocidal properties, the adequate treatment of syphilis had always been attended by danger of toxic effects from the remedies used. These dangers were enhanced by any treatment method in which a rapid curative effect was sought by increasing dosage or by reducing the time in which a therapeutically effective dose of the selected drug was given. The war and consequent increase of syphilis in a mobile service and civilian population hastened research in the methods of rapid treatment of syphilis, as even in a disciplined community such as the British Army the long-term treatment of syphilis by neoarsphenamine and bismuth was satisfactorily completed in only about 50% of cases. This treatment was further impaired, especially in the Army, by an epidemic of the so-called post-arsphenamine jaundice.

In France, of recent years, a considerable number of venereologists almost abandoned the arsphenamines in favour of bismuth (Gaté and Cuilleret, 1945) because of a fear of the grave risks sometimes encountered. This retreat from the arsenicals was sufficiently great to call for a plea for reason in the matter by Milian (1945).

The advent of penicillin, which appeared to promise cure of early syphilis in a short space of time and without producing any dangerous toxic effects, was therefore hailed with great enthusiasm. It needs at least five years to assess the value of any method of treating early syphilis, and therefore the dosage and treatment schedules recently employed for penicillin have of necessity been experimental. The experiments have, however, been on a large scale and allow of certain conclusions and assumptions.

EARLY SYPHILIS

The treatment of early syphilis has so far been carried out mainly by multiple intramuscular injections using aqueous solutions of penicillin. With this method, almost independent of the total dosage used, immediate results are the same—*Sp. pallida* disappears from surface lesions in about twelve hours, lesions heal quite rapidly, and positive serological reactions tend to reverse towards negative. Appraisal of results depends, therefore, on the appearance of evidence of clinical or serological failure after weeks or months. The largest experiments with penicillin alone were done on the plan of giving 60 injections, one every three hours, over seven and a half days. Moore (1945) had indicated that with a total dose of 60,000 units the failure rate is 100%; with 300,000 units about 75%; with 600,000 units about 40%; and with 1,200,000 units about 15 to 20%. Very large numbers of cases have been treated in the Allied Armies by 2,400,000 units penicillin over seven and a half days. Pillsbury (1945) stated that in the American Army in Europe the infectious relapse rate was between 1 and 2% in some 5,000 to 8,000 men so treated. In the same series, in some hundreds of patients, serum tests were

Mr. A. B. Nutt asked with regard to the post-operative treatment, how soon were the patients got out of bed; he also asked what was the material used by Mr. Foster to seal the face masks to the skin.

With regard to the treatment of complicated cataract, he remembered seeing a case done in Oslo in 1937 and had been impressed by the way in which the surgeon separated the iris from the lens before extracting the lens.

Mr. Foster had mentioned the slipping of masks: if the mask were adjusted so that the upper tapes went round the ears from below, and then tied on the top of the head, it would not slip up over the eyes.

Mr. Foster, in reply, said he did not seal the occlusive towel to the skin.

He found mask tapes placed under the ears and over the forehead were uncomfortable if tight, and liable to slip if looser. The problem of steaming of glasses was not a personal one to him yet, as he wore no optical aid apart from a Bishop Harman loupe on rare occasions.

He believed that the claim that myopes did well with intracapsular extraction was not entirely novel but that it had already been made by Elschmig. (He had been unable to verify the reference).

It appeared to be implied by one previous speaker that a peripheral iridectomy was difficult after the lens had been extracted intracapsularly; this was not so. It was quite simple, but where there remained the slightest visible tendency to prolapse after eserine, he himself always performed a complete iridectomy, as there was no risk of capsular incarceration.

Although an admirer of Kalt, and a frequent visitor to the "Quinze Vingt" in peacetime, he had never been able to get apposition by corneal sutures, with comparable accuracy. After two cases of epithelial downgrowth, which he blamed on the "overlap" he now copied Lindner and employed conjunctival sutures unless there was exophthalmos.

He was interested to hear that patients might get up before the second day, as not long before his own appointment to the Leeds Infirmary restless cataract patients had been immobilized for several days after operation by a towel over the forehead passed under a sandbag by each temple. Long before this it had been conventional on the Continent to sit uncomplicated cases in a chair forty-eight hours after operation. Eventually he thought even conservative nursing staffs would welcome the shorter period in bed, as there were fewer chest and mental complications, the patients were more comfortable, and nursing was easier.

He suggested that the probable reason the patients were "so good" at Manchester, was that they were not upset by pre-operative treatment. The more they received the more excited they became. Repeated postponement on bacteriological grounds was worst of all. If patients could walk straight from out-patients into the theatre, they would probably behave if possible even better.

Dr. Duthie, also in reply, said that Mr. Williamson-Noble had raised the question of secondary cataract. He always freed the iris with the iris repositor before he proceeded to extract. Having lost many of the hospital records owing to enemy action, he circularized the patients with a view to obtaining their later history. The best letter he received was from a relative who wrote: "Thank you for inquiring about grandpa." He died last Tuesday. Until the day of his death he was drawing the blind pension. He looked this man up in his records and found that the last entry was that he had 6/9 vision. He thought he was entitled to say that that was not the kind of case that came into his series.

He had no hesitation in doing a full iridectomy if necessary.

Dr. Sinclair had taught him to get his patients up after forty-eight hours, and this was done provided the eye was quiet and the anterior chamber reformed. On the tenth day the bandages were removed and a shade was worn. The bandage over the unoperated eye was removed after twenty-four hours. He, like Mr. Foster, had been brought up on the sandbag and towel method, but he insisted that his patients must be nursed in the most comfortable position.

He agreed that the more pre-operative treatment that was given the worse did the patients become. He was brought up in a great school of clinicians, and when he started with patients they were purged and Heaven knew what else!

A question had been asked about the suture. The object of it was to bring the edges of the wound into apposition.

He added that what he had learned most from that discussion was in Mr. Foster's quotation of Sir Richard Cruise's remark about being "surgically comfortable", that was the whole secret.

satisfactory method of treatment I was guided by the American observation that there was probably a synergistic action between penicillin and arsenoxide. Dr. F. R. Selbie, whose work on animal syphilis is well known, advised me also, and the original scheme which we evolved consisted of the administration of 2,400,000 units penicillin over seven and a half days, beginning at the same time, 14 intravenous injections each of 0.09 gramme Neohalarsine or 0.06 gramme Mapharside, over twenty days. The arsenical injections were given on two days out of every three, a method known to be almost free of dangerous toxic effects.

This scheme was altered in order to reduce the time spent in hospital and the method I have used for the last nine months consists in giving 2,400,000 units penicillin in seven and a half days and 10 daily injections of 0.09 gramme Neohalarsine or 0.06 gramme Mapharside. Arsenical toxic effects are rare, and if they occur arsenical treatment ceases and the total dose of penicillin is increased to 4,000,000 units (100 injections of 40,000 units). This routine has been adopted by Colonel Copping, Consulting Physician Canadian Army, for Canadian soldiers requiring a rapid effective treatment before repatriation.

So far, 360 cases have been treated by these methods; 120 with penicillin and 14 injections of Mapharside or Neohalarsine, and the rest with penicillin and 10 injections of Mapharside.

Only about one-third of this number has been successfully followed over four to six months after completion of treatment, but so far there have been 3 cases of mucocutaneous relapse, 1 case of possible reinfection, and another of indubitable reinfection, and no case of serological relapse. Of the 3 cases of relapse it is interesting to note that 2 had previously been treated unsuccessfully for syphilis; one with 2,400,000 units penicillin, and the other with nearsphenamine and bismuth.

Major S. M. Laird quite independently, but for the same reasons as I, began about the middle of 1945 to supplement penicillin treatment with arsenoxide (400 mg. Mapharside) and bismuth (1 gramme). His successor, Major Muirhead, has told me that over 500 cases have now been so treated but a significant follow-up has not been possible. Three cases of surface relapse have, however, been seen among those followed.

These results suggest that combined therapy with penicillin and arsenoxide, although not attaining complete efficiency, is an improvement on treatment with 2,400,000 units penicillin alone. Combined therapy, judging by early results, is probably in the same order of effectiveness as the "20 day" arsenoxide and bismuth treatment and is, if done in good circumstances, almost without danger. In my series there have been a few cases of minor toxic arsenical effects and one case of encephalopathy which recovered. Three cases of jaundice, occurring about 100 days after treatment, have been noted. In Major Laird's series there was no case of arsenical toxicity.

For the treatment of patients who have relapsed after treatment with penicillin alone, I now use 4,000,000 units penicillin and a daily injection of 0.06 gramme Mapharside or 0.09 gramme Neohalarsine for ten days.

I recently began two large-scale experiments in penicillin therapy for early syphilis in the Army. The routine treatment in Army hospitals now consists either in 2,400,000 units penicillin with a daily injection of arsenoxide (Mapharside 0.06 gramme or Neohalarsine 0.09 gramme) for ten days, or in 4,000,000 units penicillin alone. 1,000 cases are to be treated by each of these methods and the results of a follow-up on such numbers should yield information of some value.

Other methods.—The great drawback with penicillin has been the necessity for hospitalization and in civil practice this has meant that its use has been curtailed. Until now, for my civilian patients at the London Lock Hospital, my scheme has been to begin treatment with nearsphenamine and bismuth on diagnosis and to have patients admitted to hospital for a week for 2,400,000 units penicillin as soon as possible. The arsenical and bismuth treatment continues in hospital and after discharge for a total of ten weeks, i.e. the equivalent of one standard course. I have only treated about a score of cases in this way in the last year, so I cannot make any assumptions about the efficiency of the method.

Ambulant treatment with one daily injection of penicillin in beeswax oil mixture is at present on trial and early results will no doubt be available in a few months. Lourie (1945) and co-workers have described a rapid ambulant method in which 600,000 units penicillin in aqueous solution are administered intramuscularly every hour for three doses on five successive days. The series is very small but the results are good. Lloyd-Jones and Maitland (1945) have also reported good results in ambulant cases using

negative at the end of six months in 98% of seronegative primary cases, in 87% of seropositive primary cases, and in 72% of secondary syphilis cases.

My own experience in a relatively small series of cases similarly treated was not quite the same. Of 67 cases no less than 10 could be classified as treatment failures at the end of a six months' follow-up, surface relapses predominating. (Table I.)

TABLE I.—EARLY SYPHILIS TREATED WITH 2,400,000 UNITS PENICILLIN AND FOLLOWED FOR SIX MONTHS.

(Military Isolation Hospital, London.)

Primary	sero-negative	17 (of which 2 relapsed)	Analysis of relapse cases :	Cutaneous	...	5
"	sero-positive	38 (of which 4 relapsed)		Muco-cutaneous	...	2
Secondary		12 (of which 4 relapsed)		Serological relapse	...	1
	Total	67 (of which 10 relapsed)		Sero-resistance...	...	2
						10

That this was not an isolated phenomenon, due perhaps to faulty technique, is indicated by the results in a series treated at the Military Hospital, Preston (Table II), and followed for six months. (Major Muirhead kindly extracted these results.) Further, Major McPhater has indicated to me that the failure rate among cases so treated at Military Hospital, Peebles, was over 10%.

TABLE II.—EARLY SYPHILIS TREATED WITH 2,400,000 UNITS PENICILLIN AND FOLLOWED FOR SIX MONTHS.

(Military Hospital, Preston.)

Sero-negative syphilis	29 (of which 7 relapsed)	Analysis of relapse cases :	Muco-cutaneous	...	14
Sero-positive syphilis	70 (of which 9 relapsed)		Unsatisfactory serological response	...	2
Total	105 (of which 16 relapsed)				16

A recent check at the Central Syphilis Register at the War Office showed that in 270 cases of early syphilis, treated with 2,400,000 units penicillin and followed over six months, the failure rate was about 8%. At the same time a check was made on the same number of cases treated by the "20 day" arsenoxide and bismuth method, and the failure rate was only 2%. Dr. J. E. Moore, in a personal communication, has told me that the failure rate was 7% in a large series of cases followed for eight months after similar treatment with penicillin. Finally, in the American lay Press (Shalett, *Look Magazine*, 13.11.45) it has recently been stated that, judging from Army records, some 10 to 15% of cases of early syphilis will relapse in an infectious form in three to nine months after treatment with 2,400,000 units penicillin.

Relapse and treatment failure.—Relapse or failure of treatment may be manifested in a number of ways.

(a) *Surface relapse*: Cases are sometimes seen where the chancre fails to heal completely and later breaks down again. Oftener the chancre heals completely, but, after a latent period, reappears on the original site and may then be accompanied by signs of secondary syphilis. Sometimes relapse phenomena are entirely "secondary" in type, the primary lesion remaining healed. Evidence of serological relapse often, but not always, precedes or accompanies surface relapse.

Relapse lesions are often small and discrete and may escape notice by the patient. The ano-genital area should always be inspected closely at routine follow-up examinations as it is a common site for relapse phenomena of the condylomatous type.

In the cases I have seen surface relapse has occurred between 59 and 200 days after treatment, with an average of 83 days.

(b) *Serological relapse*: In successfully treated cases of early syphilis, positive serum tests reverse to negative in two to five months. Serological relapse is diagnosed when serial quantitative serum tests show an increasing titre of positivity following a phase of negativity or declining positivity.

(c) *Sero-resistance*: This state is diagnosed at the end of an arbitrary period of six months in cases where serial tests have shown a maintained level of positivity. In some cases there is no decline after treatment; in others there is a decline to a lower maintained level.

(d) The less common phenomena of treatment failure include neuro-recurrence, ocular and osseous relapse, and persistence of *Sp. pallida* in surface lesions in spite of treatment.

Combined treatment.—I was soon dissatisfied with the results in early syphilis treated with 2,400,000 units penicillin alone, as the early infectious relapse rate was much higher than that seen with the "20 day" arsenoxide and bismuth treatment. In planning a more

The lines of investigation of treatment methods must now, with the return of men to civil life, be turned even more towards a search for a method suitable for ambulant patients. The solution may be found in the use of vastly increased doses of penicillin in aqueous solution as already explored by Lourie (1945), or in the use of retarding substances. It has already been shown that gonorrhœa can be cured by very large doses of penicillin by mouth, and this route may be found also to have its uses in syphilis.

The long-term method of treatment of syphilis is now considered almost with contempt by some venereologists because of the impossibility of making all patients continue regularly under treatment; and penicillin is hailed because a rapid and complete treatment is possible. However, the patient treated inadequately by the old system was often a danger only to himself, whereas the patient who is not cured by a single inadequate penicillin treatment and who develops cutaneous relapse lesions is a danger to the community.

Experience has usually caused these rapid attempts to cure syphilis to become lengthened when the first flush of enthusiasm was spent. Penicillin may be the exception, but it is too soon to say.

The Anglo-Saxons have always been more optimistic about the prognosis of syphilis than have the French. Even now, knowing something of penicillin, Professor Gougerot (1945), with forty years' experience behind him, dictates that the life of a syphilitic should be divided into five periods; (1) a treatment of attack (with the most potent remedies available, lasting several months); (2) a treatment of consolidation (with bismuth, mercury, &c., lasting two to three years); (3) a period of observation and tests of cure; (4) a treatment of assurance against the disease (ten to fifteen years); and (5) a period of observation which lasts all the rest of the patient's life. Touraine (1945), another of the elders in French venereology, says of penicillin, "we still do not know if the results are of a superficial nature (he uses the excellent expression, *blanchiment*) or if it is a cure", and his advice (in a general way) is to treat intensively at the start and to prolong treatment in courses, taking no account of apparently rapid early superficial success.

I think we all agree that some comparatively rapid method of treatment is necessary to combat the lack of enthusiasm of the patient for repeated visits to hospital. Whether this can be found in penicillin alone, in single or repeated courses, or in some method of combined therapy, is a problem which, I fear, will not be settled for some time to come.

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Dr. F. R. Selbie recounted some of the results he had obtained at the Bland-Sutton Institute of Pathology, Middlesex Hospital, on the effects of penicillin and penicillin combined with arsenicals in experimental rabbit syphilis. At first, an attempt was made to see whether a short course of penicillin would be as effective as a single dose of an arsenical and secondly the dosage required when penicillin was combined with arsenic in treatment was studied. On the whole he considered his results had been disappointing partly owing to the variability of the disease produced but they showed that penicillin had a rapid and dramatic therapeutic effect comparable to that of the arsenicals. This effect, however, was not as lasting as the effects obtained with the arsenicals and he thought that if, in clinical practice, penicillin was combined with arsenical drugs those latter should not be cut down to less than half the usual dose or perhaps even to two-thirds.

Mr. A. J. King: In some ways it was a misfortune that penicillin was found to be effective in the treatment of syphilis while a major war was in progress. A preparation apparently more effective than the organic arsenicals, though practically free from toxic effects, was perhaps the long-awaited ideal; but obviously to assess it for the treatment of a disease like syphilis required time, care and restraint. In the event, the pressure of circumstances was such that penicillin was introduced as the routine unsupported treatment of early syphilis in the United States Army in June 1944 and in the British Army in October 1944. The remedy was untried, and to use it as a routine under the conditions of movement

penicillin in single daily doses of from 300,000 to 500,000 units by intravenous or intramuscular route to a total of from 2,400,000 to 5,000,000 units.

LATE SYPHILIS

Osseo-cutaneous late syphilis of the acquired or congenital type reacts rapidly to penicillin in most cases, and I have had good clinical results with gummata of the testicles. Interstitial keratitis reacts equivocally to penicillin as it does to other remedies. I have treated two cases of aortitis and one of aneurysm of the femoral artery with penicillin. They were not prepared in any way beforehand, but in the first forty-eight hours individual doses were of only 10,000 units. There was no evidence of therapeutic shock. Penicillin is not spectacularly successful in producing reversal of positive serological tests in cases where the arsenicals have failed in this object.

Penicillin given by parenteral injection in the standard doses does not penetrate to the cerebrospinal fluid in demonstrable quantity, but clinical effects are manifested in spite of this. Only when very large doses are given, such as those used by Lourie (1945), is there demonstrable any penetration into the cerebrospinal fluid. The introduction of penicillin into the cerebrospinal fluid by cisternal puncture as used by Neymann and others (1945) in cases of general paralysis of the insane appears to be a hazardous proceeding. They report two deaths from chronic penicillin encephalopathy.

Clinical improvement has been reported in varying percentages of cases at all stages and in all types of neurosyphilis. Nelson and Duncan (1945) have reported on early syphilitic meningitis; Gammon, Stokes and co-workers (1945) on all varieties of neurosyphilis. The latter authors again draw attention to the rapid changes obtained in abnormal cerebrospinal fluids. These improvements, most marked with regard to cells and protein, begin in a few days and continue up to four months after which no change can be expected. The doses they used varied from 1,200,000 to 4,000,000 units and the larger the dose, the better the result. Increasing the time of treatment as well as the dose improved results and the best results of all were obtained in cases where two courses were given. They suggest giving penicillin in courses, and it will have to be determined whether the courses should be closely approximated or whether the second course should be given at the end of four months when all effects of the first will have finished.

My own observations in small numbers of cases of neurosyphilis of all types confirm the observations I have just quoted. I also have treated neurosyphilis with two courses of penicillin, each of 2,400,000 units, at a week's interval and had good results (1945). The idea was suggested to me by Professor J. W. Bigger.

In the treatment of late syphilis of all types I now begin with a course of 4,000,000 units penicillin in 100 injections of 40,000 units over twelve and a half days. This may be varied a little at the start by reduction of individual doses if therapeutic shock is to be feared. After this I give a treatment of consolidation with bismuth or with bismuth and an arsenical, depending on the type of case, and lasting at least six months.

CONGENITAL SYPHILIS: PREVENTION AND TREATMENT

Lenz, Ingraham and co-workers (1944) have reported that penicillin has good effects on mother and child in syphilis during pregnancy. Miscarriage, stillbirth, and neonatal death can be averted, and infants are born apparently healthy. Platou, Hill and co-workers (1945) report good results in infantile congenital syphilis with doses of from 16,000 to 32,000 units per kilo distributed over seven and a half days.

I have personally treated no infants and only a few pregnant women. For these latter cases I have used penicillin plus a standard course of neocarsphenamine and bismuth. Only one has so far come to term and she had a healthy child.

SUMMARY AND CONCLUSIONS

Although penicillin has been shown to be an effective agent in the treatment of all stages of syphilis, judgment of its place in the general scheme must be deferred until the cases first treated have been followed for at least five years.

There is some reason to believe that the failure rate in early syphilis is inversely proportional to the dose of penicillin so that better results may be attained when larger doses are used. Possibly giving penicillin in courses may be found better than a single treatment.

Combined penicillin and arsenical therapy gives promising results and perhaps combinations with other anti-syphilitic remedies may also be effective. I have not used penicillin and bismuth alone in any scheme of rapid treatment lasting only a week or two. This was considered but abandoned after consultation with Professor Levaditi, who could not foresee any possibility of success with such a short course of bismuth.

This assessment includes all patients irrespective of the adequacy of treatment, but the basis of comparison is probably a fair one, although practically all the patients treated with penicillin must have completed their treatment satisfactorily. Irregularity of treatment and drug intolerance are hazards which are inherent in the long-term methods of treatment of syphilis, and must be accepted as such in any comparison with a treatment which is of short duration and devoid of toxic effects.

As far as the evidence goes, and that is not very far, it appears that the anticipated results from penicillin therapy, based on the few studies available, are at any rate not far short of those obtained with standard methods. For treatment which occupies little more than a week, and carries no mortality and no unpleasant effects, this cannot be regarded as failure.

Clearly most of this comparison is speculative and is scarcely justified by the present state of our knowledge. Many concurrent investigations, of the kind which Marshall has outlined, are required, with the most accurate and complete follow-up which can be obtained. An immense amount of vital information must now be available in the War Office Central Syphilis Register, and it is disappointing that the figures quoted from this source amount to no more than 270 cases. Presumably there are difficulties because of the rapidity with which men are returning to civil life, and the fact that clerical staffs are being reduced. It seems to me that there is a good case for setting up an organisation which will follow these men by letter into civil life, and do everything possible, by co-operation with the public clinics, to obtain information as to their clinical condition and serum reactions during the next few years. My own experience from a recent follow-up of patients, treated by hyperthermy for gonococcal and other forms of arthritis, and traced in civil life, is that these inquiries are seldom resented. Most patients are anxious to help and appreciate the interest which is taken. The time for such an investigation is now; the longer it is left the more difficult it will become. With a view to this meeting I went through the case cards of patients attending the Whitechapel Clinic who had received penicillin for syphilis. The result was most unsatisfactory. There were very few from the Forces—10 out of 33 male patients—and it seems as if the instructions which these men have received to continue their tests in civil life are being disregarded. The few civilians who had received this treatment were even less satisfactory from the statistical point of view. All had received injections of arsenic and bismuth in addition, and the amounts varied greatly.

As matters stand results of treatment with penicillin alone, in so far as they are known to us, are certainly not good enough for us to be satisfied with them; and Marshall has done well to initiate experiments which may help to lower the incidence of relapsing infection. His results obtained by combining penicillin therapy with forms of intensive arsenotherapy are interesting, especially when taken in conjunction with the experiments in animals which Dr. Selbie has described. His use of arsenicals is based upon modifications of the scheme of intensive treatment by which daily injections were given for approximately twenty days. It is well to remember that this form of treatment requires the highest standards of observation and nursing care. It was said by Moore (1943) to carry a mortality of 1 in 400 cases, although Pillsbury and his colleagues, who treated over 3,000 patients by this method, had no deaths. Marshall had no deaths in his present series of 360 cases, but his one case of arsenical encephalopathy was in serious danger because the mortality in this condition is 50%.

There are certain aspects of the value of penicillin which it is legitimate to stress even at this stage of inexperience. The importance of such a therapeutic measure for defaulting and unco-operative patients in civil life, and for those who do not tolerate arsenicals or bismuth or both, is obvious. The view has been expressed that the majority of early syphilitics will get well even with treatment which is generally regarded as inadequate; but a proportion will be difficult to cure even with full and adequate treatment, for immunity processes play a large part in the cure of syphilis as of other diseases—a point which seems obvious but is apt to be overlooked. It may be that when the optimum dosage of penicillin is known it will throw into sharp relief these resisting cases, which may thus be identified early in the course of the disease and treated by one of the more radical means at our disposal, such as intensive arsenotherapy or artificial fever.

To summarize, therefore, the anti-spirochætal effect of penicillin is not in doubt; but we are far from having assessed its true and ultimate place in the treatment of syphilis. Such an assessment is dependent upon the lapse of time and also upon planned investigations which seem to have been neglected in this country. Only one system of dosage has been applied in early syphilis on a scale which should yield valuable results, and the figures mentioned in this Discussion show that assessment is being left to the unaided

which then prevailed was something of a gamble. Whether the risk was justified awaits the test of time, but preliminary impressions, based on personal experience and the few reports available, suggest that success for so short and safe a treatment exceeded the expectations of all but the most sanguine.

At the same time the conditions were laid for a large and important experiment in which many hundreds of patients with early syphilis, from a controlled and disciplined group, were treated with standard dosage of a new remedy, with facilities for follow-up and observation which would never be available in civil life. It seemed that this should provide the means for a short cut to knowledge which otherwise would take years to acquire.

In the treatment of early syphilis with penicillin alone the only studies on a scale large enough to be significant are those in which the dosage of 2,400,000 units has been given in the seven and a half day period. In Marshall's series of 67 cases followed for six months, failures of treatment amounted to 15%, of which 12% were clinical or serological relapses. The experience at the Military Hospital, Preston, was similar, showing in 105 cases 15% of failures, of which 13% were clinical relapses. Pillsbury (1944) reviewed 5,000 to 8,000 cases treated in the United States Army finding 1 to 2% of known relapses in patients observed for one to ten months after treatment. In 792 of his cases the blood serum was tested six months or more after treatment and 13% had positive Kahn tests. There is no evidence as to how many of these were serological relapses and in how many the serum reactions failed to respond. This appears to be an almost identical proportion of failures, with the difference that in the British cases the percentage of actual clinical relapses was much higher. In early syphilis under treatment the persistence or relapse of positive serum reactions is so strong a pointer to the probability of clinical recurrence that this difference would not seem to be significant. The remaining evidence on this point comes from the War Office study of 270 cases treated with penicillin and followed for six months, in which the relapse rate was 8%, and from Dr. Earle Moore's personal communication to Colonel Marshall, from which it seems that relapse rate in a large series of cases followed for eight months was 7%. It is presumed that in these series the term "relapse" is intended to include clinical and serological relapses and also those cases in which the serum reactions did not respond.

If Marshall's figure of 12% of relapses in the first six months after treatment is considered in relation to the observation of the Co-operative Clinical Group in the United States, based on a large number of cases treated with standard courses of arsenicals and bismuth, that 45% of relapses of all kinds occurred within six months of the completion of treatment, it is possible to estimate that the number of relapses to be anticipated in the final assessment of Marshall's series is 29%. To this figure must be added the 2% of his cases which were sero-resistant, for the extent of this type of failure is obvious within the first six months. Thus the total proportion of estimated failures in his cases would be 31%. This may well be an overestimate if there is a close analogy between the effects of the organic arsenicals and penicillin, both of which are quickly acting remedies, quickly absorbed and quickly excreted. There is evidence that the organic arsenicals, when given alone in inadequate dosage, may shorten the latent period of relapse; it is believed that in cases treated with intensive arsenotherapy the majority of relapses occur within six months and almost all occur within the year. It is reasonable to suppose that the cycle of relapse and progression may also be hastened by penicillin.

In order to assess the significance of these estimated figures it is of interest to compare them with statistical studies relating to the long-term treatment of early syphilis with arsenic and heavy metal. The most comprehensive of these studies is that of the Co-operative Clinical Group from the publications of which (Stokes *et al.*, 1932) the following table is adapted:

EVIDENCE OF RELAPSE AND RESISTANCE TO TREATMENT IN 3,244 CASES.
(CO-OPERATIVE CLINICAL GROUP.)
(The Figures are Percentages.)

Results of treatment	Sero-negative primary	Sero-positive primary	Early secondary
Relapse, serological... ..	6.4	0.0	10.7
Relapse, clinical... ..	2.6	2.7	2.0
Neuro-relapse, clinical or serological... ..	1.8	3.0	4.4
C.S.F. persistently abnormal... ..	.6	1.0	1.3
Positive blood W.R. irreversible for 1 year or less... ..	1.2	7.5	5.5
Positive blood W.R. irreversible over 1 year... ..	2.6	7.0	7.8
Totals... ..	15.2	32.0	32.6

Average of failure in 3 groups = 20.6 %.

date. All cases described have been primarily diagnosed by the finding of the *Sp. pallida*. Out of a total of 370 cases of primary and secondary syphilis, 295 cases are available for evaluation purposes—the 75 cases not included, being all of less than one month's surveillance. Of the 295 cases, there were 105 with a surveillance period of from one month to four months inclusive (77 of these cases are already negative) and 190 cases from five months to seventeen months. We had 6 relapses in 223 primary cases, and 12 relapses in 72 secondary cases, a total of 18 relapses in 295 cases, or roughly 6%. This arbitrary period of four months was taken as all our cases are kept in their home depot for surveillance for this length of time prior to being drafted. Whether by the I.V. or I.M. method the conclusions arrived at, based on the results of our work point to the fact that, with a total dosage of less than 3.9 M.U. in primary syphilis, and a total dosage of less than 4.8 M.U. in secondary syphilis—relapses will occur. With the doses now considered to be minimal, i.e. 13 daily injections of 300,000 units or 8 daily injections of 500,000 units for primary syphilis, and 16 daily injections of 300,000 units, or 10 daily injections of 500,000 units for secondary syphilis, there have been no relapses to date.

Miss G. M. Sandes: I have used penicillin in the treatment of congenital syphilis but do not advise it in every case. Congenital syphilitics under the age of 10 years may be grouped as: (1) The florid types. These in my experience do well, but it is advisable not to give penicillin to the infant when it is first admitted acutely ill. When we did this we found that there was an acute exacerbation of symptoms, especially catarrhal, and that these infants tended to be "drowned in their own secretions". For this reason we now defer giving the penicillin until ten to fourteen days later, when three or four doses of intramuscular acetylarsan for children will have been given. Penicillin is then administered by 20,000 units intramuscularly, three-hourly dose day and night (omitting one dose at night because of sleep) until a total of half a million units have been given. This was the procedure if the infant was under a year. From 1 year to 5 years old, a child received a total of 750,000 units of penicillin.

(2) Milder types with few signs but with a positive blood Wassermann reaction. I do not consider that I can adequately assess the value of this treatment in these milder cases.

(3) Congenital syphilitics with bone affections respond rapidly to treatment with penicillin. Radiologically the lesion "melts away" but arsenic and mercury or bismuth therapy must be continued subsequently for some time, in the present state of our knowledge.

Finally, there are some cases which have caused me great anxiety, namely, women married to men who had been assured that the treatment with penicillin alone which they had received in the Forces had been sufficient to effect a cure. When pregnant the woman's blood Wassermann reaction was strongly positive in each case. Intensive treatment to the mother produced one congenital syphilitic baby but the other two mothers fortunately were delivered of healthy children.

I should like to ask Dr. Marshall about the condition of the cerebrospinal fluid in those patients which he mentioned where the blood Wassermann reaction remained persistently positive.

Colonel L. W. Harrison supported Brigadier Osmond's view that the analogy with "606" was a strong one. He would remind them that the results obtained by the workers at the Military Hospital, Rochester Row, and by Gennerich at Kiel between 1910 and 1914 showed that with less than three months' steady treatment with an arsphenamine preparation and heavy metal one could achieve a very high percentage of cure, approaching that obtained with the year's treatment that was routine to-day; the additional courses after the first might be likened to the disproportionate amount of fuel required to squeeze out extra knots in a ship's speed after attainment of the optimum. He described investigations on substances which retarded absorption of penicillin, in which 24 centres had collaborated with him. He had used suspensions in arachis oil containing 2, 2.5, 3.2, and 3.5% beeswax, and in ethyl oleate containing 4, 5, 6, and 7% beeswax. These had been in a concentration of 50,000 units per c.c., but he had also used stronger concentrations of penicillin in ethyl oleate with 4% and 5% wax. Generally, in agreement with Kirby *et al.*, there had not been a very significant difference in the proportions of penicillin he had found in blood serum and urine after injection of these suspensions, but he had thought that 3.5% wax in arachis oil was better than 2.5% and that 6% wax in ethyl oleate was at least as good as 3.5%

enterprise of individuals, rather than planned on the national scale, which the size of the problem and the nature of the material demand. As far as present investigations go they indicate that the system of treatment which has been used may be expected to produce a proportion of successful results similar to those obtained with standard long-term treatment with arsenic and heavy metal, even though the hazards of irregularity and toxicity are removed. The urgent need is to take steps to assess by means of follow-up the large number of cases which has been treated in the Services during the past eighteen months. On the basis of this knowledge other schemes of treatment can be planned. The possibility of synergistic action between arsenicals and penicillin is at present no more than an idea, though the place of combined treatment for syphilis requires investigation, as do many other problems. The urgent need of the moment is to explore and exploit to the full the outstanding virtues of penicillin itself, namely its speed, its immediate efficiency and its apparent lack of toxicity.

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Brigadier T. E. Osmond thought the papers were most valuable particularly in view of the wide experience of their authors: he would have preferred the subject to be entitled "The Place of Penicillin in the Treatment of Syphilis" because penicillin alone would not cure all cases. He compared penicillin with arsenic in that both tended to fail to live up to the early hopes reposed in them, and with both, bigger and bigger dosage was used.

Results obtained in the American Army were much better than those in the British—there appeared to be no explanation of this. Relapse and reinfection were difficult to distinguish; the latter should always be suspect; the causes of the former might be several—the spirochate being encysted in avascular tissue, or it might have a resistant stage in its life cycle or there might be "persisters" as suggested by Professor Bigger. He did not know whether penicillin should be given in long or short-repeated courses or supplemented with arsenic or bismuth, or both, but he thought that bismuth had been rather overlooked in favour of arsenic; both penicillin and arsenic were excreted rapidly whereas bismuth remained in the tissues over long periods.

To estimate the effect of treatment, one needed a good quantitative test and a central laboratory should guide such testing.

He thought penicillin a wonderful remedy, but it should be subjected to controlled investigation and not used haphazard.

Surgeon Captain T. R. Lloyd-Jones, R.N.: It has been our aim at "Navy Wing", Cosham, since August 1944, to evolve an efficient scheme of treatment which could be used on ambulatory patients. Earle Moore has put forward certain schedules of treatment, some with penicillin alone, others combined with different doses of arsenic, &c., to be carried out by different groups. We chose to carry out our investigations with penicillin alone, and also decided to base our work on the single daily injection method.

Our first experiments were to find out what single minimal dose would remove *Sp. pallida* from surface lesions and would ensure that they would still be absent over a period of twenty-four hours. Doses below 160,000 units were found to be inconsistent in this respect, but with this dosage the *Sp. pallida* disappeared in an average of eleven hours and remained absent at twenty-four hours. We took as our starting point the standard dosage of 2.4 mega units spread over seven and a half days as used in the U.S.A., but the 160,000 unit dose daily would have required a period of fifteen days. In order to adjust the time dose relationship we stepped up our daily dose to 300,000 units entailing eight days' treatment. At the commencement of our work the intravenous method was adopted and as experience and results were obtained the total dosage had to be increased according to the stage of infection, as relapses had occurred. The results of the work done by the intravenous method were most encouraging but in view of the simplicity of administration by the intramuscular route, with the probable elimination of any tendency to therapeutic shock, the intravenous method was discarded in favour of the intramuscular method in March 1945, and this method has been in use since that

Section of Dermatology

President—SYDNEY THOMSON, M.D.

[January 17, 1946]

DISCUSSION ON PHOTOGRAPHY IN RELATION TO DERMATOLOGY

Dr. A. C. Roxburgh: My objects in suggesting to the Council of the Section that this meeting should be devoted to photography in relation to dermatology, were three in number.

First, to encourage the members of the Section to use photography more for recording their interesting cases for publication, or their typical ones for teaching purposes.

Secondly, to show that it is easy to take quite passable and useful photographs with quite simple apparatus.

Thirdly, to show what can be done by experts in the way of representing skin diseases by photography, either in black and white or in colour, in prints and transparencies.

For record and teaching purposes I find ordinary black and white glossy half-plate prints the most convenient, for it is easy and cheap to make as many copies as desired. For record, they can be put in with the patient's notes, and for teaching they are handed round the class who can study and compare them at leisure. Really good colour prints would be better still, but they are very expensive. In many the colours are inaccurate and the detail indistinct. Transparencies, though better than most colour prints, are much more difficult to demonstrate as they require a darkened room.

The camera I use is an ordinary Rolleiflex twin-lens reflex taking 12 pictures, each $2\frac{1}{4}$ in. by $2\frac{1}{4}$ in., on the ordinary size 20 Selochrome film. I use a wire cable release to avoid shaking the camera; a lens hood to keep glare off the lens and two Proxar lenses for close-up work. For light, I use two "Photofloods" in holders with white reflecting surfaces, one as a main light and the other, farther away, to light the shadows. A dark screen makes a good background. A Weston electric exposure meter is a great help but I find that nearly all my photographs are taken at a fifth to a tenth of a second at f 5.6 to f 6.3. A notebook for recording patients' names and ages and details of the case, lighting, and exposure, is essential.

It is important to use ortho- and not pan-chromatic film as pan-film renders reds too light and not sufficiently in contrast with the normal skin. I always develop and enlarge my photographs myself as I find that only in that way can I get the prints to show the particular details required.

Squadron Leader H. Mandiwall: The ordinary technique in black and white photography applies equally to colour. The only difference is that the negative used instead of being ortho- material is Kodachrome. All my work in the past has been done with a Leica 35 mm. camera with Kodachrome film.

in arachis oil. After an injection of 300,000 units in oil-wax one could usually reckon on finding penicillin in the blood serum for twelve to sixteen hours, but he had not found it often in the serum at the end of twenty-four hours. On the other hand he had commonly found it in the urine seventy-two hours after such an injection, and sometimes at the end of ninety-six hours. He thought that the finding of Kirby *et al.*, that there was a longer hold-up after subcutaneous than after intramuscular injection, was important, and it seemed to him likely that the deep subcutaneous route would prove preferable to others. There was no clear evidence to show how much or for how long an assayable amount of penicillin must remain in the blood. He thought that Kirby's results in early syphilis after giving a daily dose of 300,000 units in oil-wax for eight days indicated that it was not necessary that an assayable amount of penicillin should remain in the blood throughout the period over which the penicillin treatment of syphilis was spread, and he had hitherto recommended clinics using the oil-wax suspensions to give a daily injection of 300,000 units for eight days, as the penicillin contribution to the treatment of syphilis. In a recent circular, however, he had suggested that, if practicable, two injections of 300,000 a day for five days might prove to be a more efficient course.

The strength of penicillin in the suspensions which he had tested hitherto had mostly been only 50,000 units per c.c., because of the relatively low potency of the product. Purer penicillin was shortly to become available and the investigation was to be continued with suspensions containing 100,000 or more units per c.c. Theoretically, the tighter the penicillin was packed into the dose, the slower should be the absorption; on the other hand one had to see that the viscosity was not such as to make administration too difficult and waste of the suspension through adhesion to the vial unduly great. He would express his indebtedness to his collaborators. His part in the work had been to devise the suspensions and do the tests for penicillin on which he had commented. Some collaborators had reported brilliant clinical results following the course of eight daily injections of 300,000 units.

Dr. J. Marshall (in reply to Miss Sandes): In the British Army the surveillance tests after any rapid treatment (whether by penicillin, arsenic or both) include an examination of the cerebrospinal fluid six months after completion of treatment. Lumbar puncture was also performed as a routine in any case of relapse seen in my hospital. Some hundreds of such tests have been performed and I have not as yet encountered any case in either group in which abnormalities in the cerebrospinal fluid were demonstrable.

Lighting is artificial by means of two or more "Photoflood" electric light bulbs. When using artificial light for colour film the illumination must not be mixed, as a mixture of daylight or ordinary electric light with "Photoflood" will spoil the colours entirely. For colour flat lighting is best; occasionally in black and white work oblique illumination may bring out some particular detail better.

Exposure times (using an $f\ 3.5$ aperture) are $1/30$ th second for colour, using Kodachrome A film, and $1/40$ th to $1/60$ th second for black and white panchromatic film. Alternatively you may, instead of reducing your exposure time for black and white film, close down your lens aperture slightly instead. Many of your patients will not keep still, and therefore you must use as fast an exposure as possible. It is impossible to get a good picture of any kind, say of an unruly infant with scabies, with an exposure of $1/5$ th second! For close-up work (between 2 feet and 6 inches) I use a "Nooky" close focusing device which is a coupled focusing attachment which corrects simultaneously for parallax. Parallax errors are liable to occur when taking close-ups due to the fact that you see the object through one aperture (the view-finder) and the camera takes the picture through another in a different plane (the lens). It is liable to be very marked indeed when taking at distances under 18 inches, and you may find that you have completely missed your particular target if you do not compensate for parallax. In the Reflex Kōrelle camera there is no need to compensate for it, as it uses the same lens aperture for both viewing and taking the subject.

The background used in taking colour photographs of the skin in its true tint is very important. I have found that a blue-coloured one is very effective, possibly because blue is complementary to red.

Photomicrographs in colour require no expensive equipment, only a camera, an ordinary microscope and one "Photoflood" electric light bulb (*see Proc. Roy. Soc. Med.*, 1942, 35, 700). The method is as follows:

The section is placed and focused under the microscope in the ordinary way (this must be done by a normal emmetropic eye, and if you have to wear glasses yourself you must get someone else with normal vision to do this), then the microscope with the slide in position is tilted into the horizontal position and the reflector adjusted to give good illumination. The miniature camera is brought up to the ocular of the microscope in the same horizontal plane until it just touches it firmly. All extraneous light is excluded by means of some suitable covering, e.g. a piece of dark cloth wrapped round the junction. Film used is Kodachrome A (for artificial light). One "Photoflood" light is used and reflected as described above, instead of any other source of illumination. Camera lens is set for infinity, aperture $f\ 3.5$ and exposure $1/5$ th second.

I have constructed a home-made apparatus for clinical work which carries the Leica, or other camera, in the centre, together with the necessary illuminating outfit, which can be moved about in any direction. This has been in use by me for several years, both in hospital and private work.

[Black and white and coloured dermatological photographs and photomicrographs were then shown.]

Mr. P. G. Hennell: My experience of colour photography covers approximately twelve years, using all the proprietary processes. As a professional photographer I am biased against 35 mm. equipment, although it has certain advantages for working in confined spaces. For quality I think the largest camera possible should be used.

The first slide showed a diagram of the internal construction of a colour camera originally invented in Germany and now manufactured in America. The $\frac{1}{4}$ plate negatives used allow enlargements up to 20 in. by 30 in., without loss of register. The next slide showed the Speed Graphic Camera, which I recommend for use with Dufay and Kodachrome colour film. The complete outfit contains a synchronized magnesium flash gun, and the latest model is fitted with a plastic lens, the definition of which is finer than that of any lens I have used hitherto.

Using the one-shot colour camera I light the subject with a magnesium flash gun, consisting of a sashalite pistol grip containing 4 U2 batteries with a 16 in. reflector, which takes up to 5 large sashalite bulbs, wired to ignite simultaneously. The acetate screen on the front contains the blue filter which corrects the light of the flash bulbs to daylight, for which the colour camera is balanced.

This equipment was ideal in Italy as I was able to work independently of any electrical installation. Another type of lighting worthy of serious consideration by those establish-

The technique is very simple and an ordinary amateur can record cases in colour without sending the work to outside photographers. It is advantageous to have a camera at hand to record your cases, treatment and results at various intervals. In spite of the very good black and white photographs which we have seen published in books and magazines, I think that colour photography brings out more detail and gives more realistic clinical pictures. The skin lesions have a colour of their own and so why not record them as such; besides a colour photograph, especially from the teaching point of view, impresses the mind to a very great extent.

[Colour slides were then shown.]

A meter to determine the exposure is very important in colour work and once you have standardized exposures, by copying a coloured chart, you know your results will be correct at all times.

Mr. J. E. Andrews, A.R.P.S., *Medical photographer, London County Council*: When a doctor at any one of the London County Council hospitals is desirous of having photographic work done he simply sends a request form to the central photographic laboratory. The medical photographer then goes along to the hospital to do the work required. I think one really well-equipped photographic laboratory can maintain an efficient service to several hospitals. All photographs are the copyright of the London County Council.

I have found that a half-plate camera with at least four lenses having focal lengths of 12 in., 8½ in., 6½ in., and 4¾ in., comes very near to perfection for most branches of medical photography, particularly in my own case where most of the work is done at the bedside and not in a room set aside for photography.

The camera is clamped to the top of a pair of steps about 6 ft. 6 in. high enabling the camera to be brought over the patient lying in bed. A "Photoflood" lamp with 6 feet of flex, plugs in to the existing light fitting over the bed. By interchanging the lenses I can photograph full-length figures or close-ups. I prefer to use cut film because it is lighter than glass plates and there is no risk of breakage. About 70% of my pictures are taken on a medium-speed orthochromatic emulsion.

The difficulty of photographing very small fields and cavities led me to devise the arrangement of a ¼ plate camera mounted on a board with the lens extended and fixed at a point, so that all objects at the opposite end of the board were sharply defined on the plate. The lens is stopped down to f 6.4, in order to produce great depth of focus. The lighting is by a flash bulb fixed just behind the lens and in line with the optical axis. With this unit I can get thoroughly sharp pictures of the inside of the mouth or similar subjects, because, if the patient moves, the entire unit is moved with him.

[Lantern slides of patients photographed by the bedside method and the fixed focus camera described, were shown.]

Dr. F. A. E. Silcock: My own methods of doing clinical dermatological photography are based on many years of practical work in black and white and of seven years of colour photography.

I use a Leica camera with coupled range-finder and focusing device for 35 mm., and a Reflex Korelle for 2¼ in. sq. pictures. Both can be used for black and white, but the former only for artificial light work (Kodachrome A film) and the latter for Dufaycolour. I prefer Kodachrome film for colour. The Reflex Korelle is a single lens reflex type camera in which there is a single lens, through which one both views and takes the picture, a mirror being set at an angle of 45 degrees (which reflects the picture), and this swings out of the way at the moment of exposure. You thus see exactly what you are going to take.

It is essential to have a good lens and I use an aperture of f 3.5. This allows for fast work and good depth of focus. For close-up work anything, say, from a distance of 2 feet to 6 inches away, it is necessary to use either supplementary lenses or an extension tube, both being methods of decreasing the focal length. Against using supplementary lenses is the fact that you require a number of them and they will only work at their fixed focal distances. This is a great drawback in taking a moving object whose distance is changing rapidly. I therefore prefer an extension tube. This is a short length of metal tubing, about half an inch in length, which is inserted between the lens and the body of the camera. Its use does not necessitate any increase in exposure time as supplementary lenses do.

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ing clinical photographic units is the "Kodatron" type of gaseous discharge lamp. With this lamp one can fire upwards of 5,000 flashes without replacing the flash tube, from which the light is emitted. The effective length of the exposure is approximately a 30,000th of a second, and for this period the brilliance of the light has been estimated at approximately that of 40,000 100 watt lamps. Owing to the high speed the brilliance appears to the naked eye to be less than that of an ordinary magnesium bulb.

For photographs made in the operating theatre I prefer to use blue or green sterile drapes, these colours tending to isolate effectively the operative site to be photographed.

Other slides were shown depicting scenes in the underground air-raid shelters in Naples, where there had been a serious outbreak of typhus. These photographs were made with the Speed Graphic Camera and Kodachrome Film. There were also slides showing D.D.T. being sprayed on the civil population at the railway station.

Other slides showed examples of the new types of colour photography now being produced in America, notably amongst which were examples of the Kodacolor colour negative from which an unlimited number of prints on paper can be made.

Unfortunately, there has been a great deal of exaggeration in the textbooks in the reproduction of colour, and perhaps for many purposes the black and white photograph is still the best. However, I do think that the advantage of colour photography lies in its ability to reproduce shades too delicate to be shown in black and white. If you wish to exaggerate you can do it much more successfully in black and white than in colour, but in certain conditions accurate colour photography is the only satisfactory means of reproduction.

I understand that British firms are intending to manufacture gaseous discharge lamps, and I think the speed at which they will be available will be dictated largely by the demand.

In answer to a query regarding plastic lenses, I have not experienced any scratching; the definition is quite remarkable. I have not used another lens which gave as good a performance at the aperture of 4.7 at which the Italian shelter photographs were made. They are not readily available in this country yet, and those that are have scarcity prices attached to them. Likewise there are people who will pay £100 for a Leica or Contax camera. In my opinion there will be American cameras of equal performance for something in the region of £20 on the European market before very long.

Mr. C. H. J. Bishop: The cost of reproduction of photographs in colour in a magazine or technical journal may seem out of all proportion to the original cost of the photograph, but we have to bear in mind that the colour print has to be separated into four sections, into the three primary colours and black. The charge for the block is reckoned at so much per square inch, and an average sized block of, say, 11 in. by 7 in. costs about £30.

The block-maker can make or break one's most beautiful work—more often than not he breaks it! The reproduction is often nothing like the original, and frequently is quite useless for medical purposes. There is only one way to obviate all this, and that is close association with the block-makers. My own experience of block-makers is that unfortunately at the present time they are mostly elderly men and they are colour-blinded by their own peculiar conditions. Quite a number of printers are, to all intents and purposes, colour-blind because they are so accustomed to work under arc light that they do not know daylight when they see it.

To reproduce satisfactorily, special filters are required which the block-maker does not have and if you tell him you want narrow cut separation, he will not like it at all.

Therefore, if you are going to publish colour photographs which are to be anything like the original, you must insist that the man who does it knows what he is doing. You will certainly not reach the level of the American publications in the matter of colour reproduction until you spend more money on block-making.

Dr. F. A. E. Silcock: With regard to the comments by Mr. Bishop on coloured blocks, I think it might be done by getting reproductions of your 35 mm. or any other size prints and dealing with them like a collection of stamps. You could give them numbers and if, at a later date, a better specimen came along, remove the old picture and replace it.

Mr. Bishop: It is true we have had six years of war and our printing machinery is not what it was and certainly not what the American machinery is, but when we get going

properly and bring our machinery up to date, I am convinced we shall do as well as the Americans. Apropos of the false tints sometimes found, the Dufay Company has produced a series of filters and they will tell you what combination to use. The background is a problem which wants careful watching, otherwise you can completely ruin the picture by the choice of an unsuitable colour which may reflect on to the subject and degrade its colouring.

[February 21, 1946]

? Poikiloderma Jacobi: ? Atrophic Lichen Planus.—A. C. ROXBURGH, M.D.

P. B., male, aged 57. Patient of Dr. Sears of Lyndhurst, Hants, seen on January 9, 1946.

For twelve to fourteen years reticular arrangement of red, atrophic skin on front of forearms, from wrists to elbows (fig. 1), and over whole of feet and ankles except toes (fig. 2). No definite papules but a slight suggestion of them in shiny polygonal islands between the skin furrows on forearms. In last twelve months has from time to time had blisters at sides of each tendo Achillis, one present when seen and another, ascribed to a rubber boot, on dorsum of one foot. No lichen planus in mouth or on penis. Teeth very bad. Otherwise healthy. No symptoms except in two weeks up to January 9 "pins and needles" in both hands, lately only in right thumb and index finger.

Dr. J. E. M. Wigley: I think this is the variety of parapsoriasis described by Macleod and others as parakeratosis variegata (J. M. H. Macleod, *Diseases of the Skin*, London, 1920, p. 847).

Dr. G. B. Dowling: I have seen a small number of these cases. They seem always to have the same distribution, affecting especially the outer aspect of the forearms and ankles. The cases I have seen have been subjects over 50. The condition was described in 1926 (C. D. Freeman, *Arch. Derm. Syph.*, 1926, 13, 489) under the title of erythematous lichen planus elsewhere, and there is always the characteristic distribution on the forearms and ankles. I have thought that the condition, itself very well defined, can hardly be identified with any named dermatosis, and may be an entity.

Dr. R. T. Brain: The clinical appearances are suggestive of poikiloderma, although the distribution of the lesions is unusual.

Patchy Punctate Pigmentation.—A. C. ROXBURGH, M.D.

Recurrent attacks of patchy, scaly erythema and purpura followed by pigmentation. Case shown at British Association of Dermatology meeting July 6, 1945. No diagnosis then arrived at (Jacobi's poikiloderma and angioma serpiginosum suggested) (*Brit. J. Derm.*, 1946, 58, 26).

Miss P. L., aged 22. Clerk.

History.—(1943 Summer): Noticed brown patch right side of neck.

1944 (Summer): Fresh lesions began to appear.

1945 (July): A number of symmetrical pigmented areas 2 to 3 in. in greatest diameter, of irregular shape, smooth or slightly scaly, covered with dark brown points like hæmorrhages being absorbed, situated on front and sides of neck, over each deltoid, front and inner side of each upper thigh and on left hip. Patches on deltoid regions (only) are stated to go repeatedly through a cycle of bright red spots "like red ink" which turn purple and then leave brown marks.

1945 (December 28): Red spots appeared on neck, arms, lower abdomen. No irritation.

1946 (January 6): Felt ill. Bed. T. 100° in day, higher at night. Enlarged glands in neck. Fresh areas of eruption.

1946 (January 11): Seen. Red, scaly plaques with sharp margins, slightly crusted in places, each side of neck including angle of jaw on right, with purpuric spots near upper margin, also symmetrically on top of shoulders and covering front, back and outer sides of upper arms. Purpuric eruption, dappled, but with smooth surface front of each forearm. Purpuric dappling lower abdomen to 2 in. above pubes, also front of each thigh and over whole of both buttocks which were tender to sit upon. Slight dappling backs of knees outer sides but flexures of elbows normal. No enlarged glands.

1946 (February 5): Seen in Royal Masonic Hospital. All redness disappeared and replaced by pigmentation, punctate in places, especially on neck. Small group of crusts lower right buttock (fig. 3).

Patient takes no drugs except occasional Beecham's pills or Epsom salts. No sedormid, adalin or phenolphthalein. Eats plenty of green vegetables. Otherwise well except for frontal headaches. Menses within normal limits. Never any redness or swelling of face or eyelids.

Investigations.—Biopsy from pigmented area left buttock.

Blood and urine examinations normal. W.R. negative.

Jaw: Unruptured wisdom tooth each lower jaw, that on left impacted.



FIG. 1.



FIG. 2.

FIGS. 1 and 2.—Dr. Roxburgh's male case for diagnosis. ? Poikiloderma Jacobi: ? Atrophic lichen planus.

FIG. 3.—Dr. Roxburgh's female case for diagnosis, showing patchy pigmentation on buttocks, shoulders, upper arms and right elbow.
(Photographs by Dr. A. C. Roxburgh.)

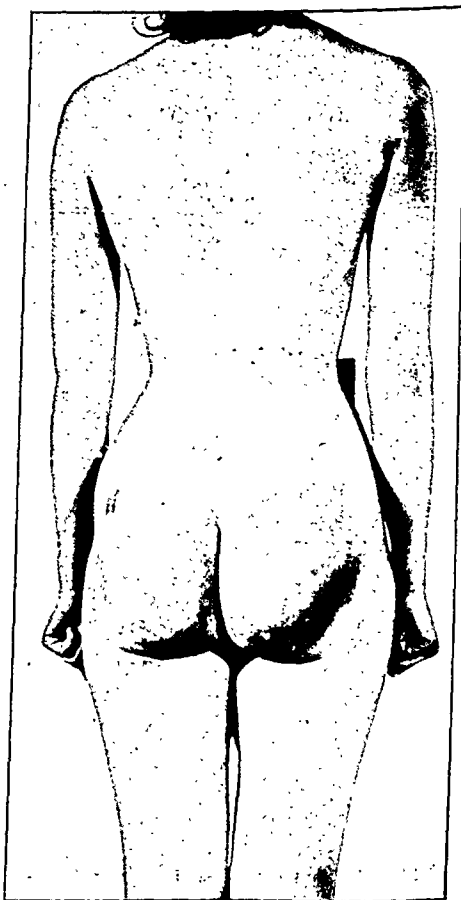


FIG. 3.

Dr. Freudenthal: Section (Fig. 3) shows capillary vessels markedly increased in papillary body. Perivascular oedema and slight infiltration. Melanin considerably increased, especially in basal layer. No iron. The sections suggest that the case is primarily a vascular disturbance which has led to an increase in melanin production.

Reticulo-endothelioma (Spiegler-Fendt Tumour).—G. W. BAMBER, M.D., and W. FREUDENTHAL, M.D.

Dr. G. W. Bamber: Mrs. R. K., aged 80, was first seen by us in December last when she said that her scalp had started to become tender and to swell two and a quarter years previously. Examination showed the right side of the vertex, the front of the scalp and the upper half of the forehead to be the site of a large reddish infiltrated plaque the surface of which was mammillated in some parts and in others resembled peau d'orange. On the forehead the boundary between infiltrated and normal skin was a sharply defined furrow. Almost half the surface of the lesion was eroded by a large ulcer that had become infected secondarily. Clinically the lesion was thought to be a neoplasm and this supposition was confirmed by the histological examination of a biopsy. Sections showed a peculiar vascular proliferation of the type described by Spiegler and by Fendt.

Her blood Wassermann reaction was negative.

The tumour consists of larger or smaller foci of densely aggregated mesenchymal cells. In some places it has a tendency to form fissures and vascular spaces, sometimes producing vessels of considerable size whose walls display a very active proliferation of endothelial cells which form a kind of lining. We think that these fissures and vascular spaces are an irregular attempt at forming lymph vessels. We regard the tumour as one arising from lympho-reticular tissue and suggest that this case should be grouped with the Spiegler-Fendt endotheliomas though we are not aware that a histological picture quite identical with this has been recorded.

Dr. I. Muende: I agree entirely with Dr. Freudenthal in that this is an affection of the endothelial lining of the vessels, but cannot accept it as being an endothelioma in the sense that it is a tumour of the endothelial cells. In my opinion it would better be described as an endotheliosis.

Dr. W. Freudenthal: "Reticulosis" covers a wide range of proliferative dermatoses. It includes Spiegler-Fendt's endotheliomas, a term generally accepted (Spiegler, E., *Arch. Derm. Syph.*, Vienna, 1899, 50, 163; Fendt, H., *Arch. Derm. Syph.*, 1900, 53, 213). It should not be confounded with Spiegler's "turban" tumours which are basal-cell epitheliomas, occasionally of sweat gland origin.

Balanitis Xerotica Obliterans.—J. E. M. WIGLEY, M.B.

C. H. A., male, aged 41. Married. Three years' history of recurring attacks of eruption about the glans penis and inner surface of the prepuce. He describes the eruption as numerous small blisters accompanied by a varying degree of discomfort. This was treated by various methods under a diagnosis of herpes progenitalis. He saw Dr. Dowling early last year who tells me that, having excluded an infection with monilia, he was still not satisfied that the condition was herpes progenitalis. The eruption seemed too nearly continuous. A thorium-X paint, containing 500 units per c.c., was applied on two separate occasions. The patient states that there was increase of the pain and swelling within twenty-four hours of each application. He was subsequently seen by a surgeon who found a balanitis with adhesions between the prepuce and glans. Circumcision was performed in August 1945 when it was noted that the adhesions were more tough than was anticipated. The wound was unusually slow in healing. The patient complains that his glans is still sensitive and sore, the remains of the prepuce appearing to him to be closely bound to the corona and giving him great discomfort on erection. He has not noticed any changes in the volume or trajectory of the stream of urine.

On examination.—The glans presents a white, shiny, slightly atrophic irregular area. The remains of the prepuce are firmly bound to the back of the corona and along this junction there is some dark pigmentation and some telangiectasia. Otherwise there does not appear to be anything abnormal.

My first impression on seeing this case was of its close resemblance to X-ray dermatitis and I was inclined to accept the patient's story of the connexion between the application of thorium X and the present condition. The amount of thorium X used seemed much too small to have produced this effect. More careful study of the lesion showed the marked resemblance of the whitish, atrophic area to the condition described as lichen sclerosus, which has been included under the group of cases of kraurosis when occurring about the vulva (Early Kraurosis Vulvæ in a Child, J. E. M. Wigley, *Brit J. Derm.*, 1944, 56, 20).

This case is, in my opinion, one of balanitis xerotica obliterans described by Laymon and Freeman and others and given the synonym of kraurosis penis. The occasional superficial resemblance to X-ray dermatitis has been noted, as well as the histological resemblance to both lichen sclerosus and morphea.

1946 (February 5): Seen in Royal Masonic Hospital. All redness disappeared and replaced by pigmentation, punctate in places, especially on neck. Small group of crusts lower right buttock (fig. 3).

Patient takes no drugs except occasional Beecham's pills or Epsom salts. No sedormid, adalin or phenolphthalein. Eats plenty of green vegetables. Otherwise well except for frontal headaches. Menses within normal limits. Never any redness or swelling of face or eyelids.

Investigations.—Biopsy from pigmented area left buttock.

Blood and urine examinations normal. W.R. negative.

Jaw: Unerupted wisdom tooth each lower jaw, that on left impacted.

FIGS. 1 and 2.—Dr. Roxburgh's male case for diagnosis.
? Poikiloderma Jacobi: ? Atrophic lichen planus.

FIG. 3.—Dr. Roxburgh's female case for diagnosis,
showing patchy pigmentation on buttocks, shoulders,
upper arms and right elbow.
(Photographs by Dr. A. C. Roxburgh.)



FIG. 1.



FIG. 2.

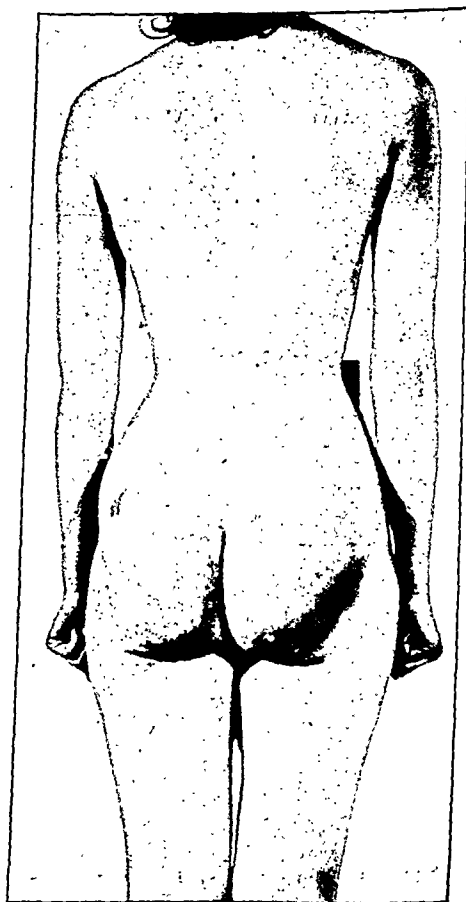


FIG. 3.

Dr. Freudenthal: Section (Fig. 3) shows capillary vessels markedly increased in papillary body. Perivascular oedema and slight infiltration. Melanin considerably increased, especially in basal layer. No iron. The sections suggest that the case is primarily a vascular disturbance which has led to an increase in melanin production.

Section of Surgery

President—ERNEST FINCH, M.D., M.S., F.R.C.S.

[March 6, 1946]

DISCUSSION ON VASCULAR INJURIES IN WAR

Mr. J. J. Mason Brown: You have done me the honour of inviting me to open this discussion because I represent the Field Vascular Injuries Centre established in C.M.F. in April 1944. Because of a variety of factors—the site of the centre in a base hospital, the impossibility of segregating all cases from a long front in one centre and the inadvisability of evacuating cases in the hæmatoma stage over long distances—only a proportion of the vascular injuries were received. It is therefore impossible to give any estimate of the relative frequency of arterial injuries or to give the views of the forward surgeon from a consideration of the work of the special unit. Table 1 summarizes the cases admitted. Apart from isolated examples the traumatic arterial lesions fall into two groups: (1) Those in which surgical treatment of the arterial injury had already been carried out—primary ligations; (2) cases of traumatic aneurysm.

TABLE 1.—CASES ADMITTED FIELD VASCULAR CENTRE C.M.F. APRIL 1944 TO SEPTEMBER 1945

Lesion	British	Others	Total
Primary ligations, larger arteries ...	21	0	21
Primary arterial suture ...	1	0	1
Arterial contusion and thrombosis ...	0	1	1
Complete division of artery ...	1	0	1
Traumatic aneurysm ...	39	39	78
Trench foot and frostbite ...	11	24	35
Vascular diseases ...	27	12	39
Total, all cases	100	76	176

From the outset our approach to the problem was influenced by the depressing results of primary ligation of the main limb vessels quoted in the surgical literature of the last war and by the statistics given by Ogilvie and Stout at a surgical conference in Cairo. That the results of primary ligation even in very experienced hands were not significantly altered in the later stages of the Italian campaign is shown by the figures kindly given to me by Lieut.-Colonel C. G. Rob which comprise the cases of arterial injury encountered by him in his last battle period with a Field Surgical Unit:

Artery	No.	Results
Common iliac	1	Died, gas gangrene
External iliac	2	1 death, 1 below-knee amputation
Femoral	3	2 above-knee amputations
Popliteal	6	4 amputations
Subclavian	1	Amputation
Axillary	2	Both satisfactory
Brachial	1	Amputation
All cases	16	2 deaths, 9 amputations

In addition during the same period six lower limb and three upper limb amputations had to be carried out for purely arterial lesions because of the prolonged pressure of tourniquets.

Stanimers (1945) at a surgical conference in Rome gave the following figures from the Eighth Army front:

Femoral ligations 31, amputations 21 or 68%
Popliteal ligations 36, amputations 26 or 72%

An analysis of the 21 cases of primary ligation in our series shows that 16 involved the brachial (6), femoral and popliteal (5 each) arteries. Six amputations had been carried out before admission, seven had limbs severely crippled by ischæmic changes and in only three cases (2 brachial) were the results really good.

The almost constant laceration and the extensive intimal damage occurring in arterial wounds make primary suture possible on rare occasions. One such case, operated on by Lieut.-Colonel G. Blackburn, was admitted. Although the lateral suture of the popliteal artery had resulted in thrombosis a day or two after operation the circulation was well established and Professor Learmonth informs me that the final result is exceedingly good.

In the M. R. C. memorandum on Arterial Injuries (1944) it was suggested that it might be possible to make a musculo-fascial barrier over the injured vessel and the records of two cases are of some interest.

On the analogy with kraurosis vulvæ, which appears to respond well to oestrogens, I gave my patient an ointment containing testosterone. He says that there is already an improvement.

POSTSCRIPT.—Dr. Prosser Thomas tells me this case is identical in appearance with the one shown by him before this Section in May 1945 (*Brit. J. Derm.*, 58, 22) under the diagnosis of morphœa of glans penis (which I regret I missed seeing). The histology reported then would seem to me quite compatible with a diagnosis of lichen sclerosus, a point made in the discussion by the late Dr. Klaber. Dr. Prosser Thomas's case appears to have followed the same course as mine and there was apparently no urethral atresia.

Dr. Prosser Thomas: The clinical appearances are the same as in my case, as was the history of blister formation, sometimes hæmorrhagic and painful. My patient had had no thorium X or other form of radiation. Freeman and Laymon (1941, *Arch. Derm. Syph.*, 44, 547) studied 18 cases of "Balinitis Xerotica Obliterans" and thought the condition could be differentiated from scleroderma histologically. They could not determine any relationship with circumcision in any of the patients, but found urethral stenosis present in all. In a later study (*Arch. Derm. Syph.*, 1944, 49, 57) they concluded that the disease is identical with lichen sclerosus atrophicans.

Dr. R. T. Brain: I regard this case as one of lichen sclerosus which may be a variety of lichen planus although Ormsby and Montgomery describe lichen sclerosus as a separate entity. It is possibly related to morphœa.

Chronic Burrowing Ulcers of the Leg.—H. J. WALLACE, M.D.

Mrs. A. G., aged 45, a Maltese. She lived in Malta until eight years before the onset of the present trouble. In March 1944 she struck her left leg on a nail while at work. This caused a small wound which bled and did not heal but gradually enlarged and was resistant to out-patient treatment for six months. The patient was admitted to St. Thomas's Hospital under the care of Mr. R. H. Boggon, and resolution occurred within the course of a few weeks. Investigations at this time showed no evidence of varicose veins: blood Wassermann reaction negative; an X-ray of the underlying bone showed slight inflammatory change only consistent with the overlying ulcer of some size. Biopsy of the edge of the ulcer showed an acute and chronic inflammation. In May 1945 the original ulcer recurred and since then other ulcers have formed on both legs. The appearance of the subsequent ulcers has been characteristic of those described as chronic burrowing ulcers of the skin and an anaerobic streptococcus has been isolated on two occasions from fresh ulcers, after further organisms such as *Staphylococcus aureus* and *B. pyocyaneus* previously isolated from the ulcers had been inhibited by local application of iodine. At no time has tubercle bacilli been found either on direct examination or culture. Since the condition relapsed some eight months ago she has been treated with penicillin and sulphonamides both systemically and by mouth, also with various antiseptic preparations, including a Bunyan bag with hypochlorite, without any permanent improvement. She is due to be admitted to St. Thomas's Hospital for further treatment probably with zinc peroxide.

I am showing this case partly because I do not believe this type of infection is common and partly because I want to prove the diagnosis is correct. A further reason for showing this patient is in connexion with the Workmen's Compensation Act. Most of these cases are described as occurring after trauma, which may vary from an abrasion to an operative wound. According to the literature prognosis is variable, but at best treatment is likely to be prolonged.

Dr. A. C. Roxburgh: It seems rather an absurd suggestion when the condition is on the leg, but the honey-coloured exudation through holes in the skin reminds me of lymphogranuloma inguinale (Nicolas-Favre disease). I do not know whether that could be considered.

Dr. A. Burrows: From the point of view of Workmen's Compensation I may point out that the original injury was to the left leg, not to the right—at least that was the story which the patient gave—but it was on the right leg that the ulcer developed.

Dr. R. T. Brain: I think it is possible that some of these obscure chronic ulcerative lesions are maintained by inflammatory reactions in the subcutaneous fat, i.e. fat necrosis.

Dr. W. N. Goldsmith: What does Dr. Wallace think is the nature of the dark purplish spots on the foot. The whole foot appears swollen. Has Kaposi's hæmorrhagic sarcoma been entirely excluded?

Dr. Wallace, in reply: Some of these bluish nodes have been observed to break down and form sinuses comparable with the sinuses formed elsewhere. There is one point to be mentioned in connexion with compensation: the original ulcer on the left leg undoubtedly followed trauma.

Treatment.—As already stated this was influenced by the results of the primary ligations we had seen. It was felt that sooner or later operation would be required in emergency and that arterial repair would be the only method likely to secure a fully functioning limb. In the early cases, therefore, suture was carried out when technically possible even in the presence of a good collateral circulation in order that technical skill might be acquired and so enhance the chances of success in cases in which it was vitally necessary. For this reason the number of suture operations is high.

The ischæmic or potentially ischæmic limb.—The limb was kept at rest outside the bedclothes and exposed to a cool environmental temperature, fans being in constant use during the summer months. It was kept in the position which was observed to give the maximum circulation, usually about six inches below heart level. The limb was slightly elevated on itself in cases in which there was peripheral œdema; otherwise it was kept level or slightly dependent to produce moderate venous congestion. Reflex vasodilatation was employed as a routine and was supplemented in the earlier cases by paravertebral nerve blocks and, after operation, by repeated doses of morphine. Penicillin was used liberally in the control of infection in the associated wounds and in wounds distal to the lesion.

Indications for early operation.—The indications for operation before the development of the maximum collateral circulation were: (1) External hæmorrhage; (2) increase in the size of the swelling associated with increasing peripheral ischæmia; (3) suppuration at the periphery of an arterial hæmatoma; (4) secondary hæmorrhage; and (5) in very large hæmatomata because of pressure on the potential collateral vessels or because of severe pain not relieved by sedatives. Mistakes were made in three popliteal lesions in which operation was carried out because of the rapid enlargement of the swelling and all were found to be gross local dilatations of the vein in aneurysmal varices—an error to which Makins (1919) drew attention in the last war. Fortunately transvenous suture was successful in each case. Emergency operations were carried out in five cases in which the lesion found was identical with that recently described by Paterson Ross (1946), viz. a mass of blood clot surrounded by fluid blood within a thin sac wall derived from the surrounding connective tissues. The emergency arose with dramatic suddenness in every case and they were regarded as cases in which the original sac had become detached from the margins of the arterial opening and further bleeding had occurred around its periphery.

Arteriography.—No complications followed its use, the technique employed being similar to that described by Learmonth (1944). This diagnostic method gives reliable evidence of the extent of the collateral circulation and may also be of value in localizing the site of the arterial injury. It is unfortunately of little value in old-standing cases of aneurysmal varix merely showing a faint outline of the grossly dilated vein (figs. 2, 3, 4). It was carried out in a few cases of large hæmatoma and here it confirms the clinical finding that there is always some circulation through the affected vessel.

Heparin.—Heparin was employed after arterial suture operations but was not employed after transvenous suture of aneurysmal varices. Its control by body-weight was very uncertain and different batches seemed to vary in their potency so that repeated estimations of the coagulation time had to be carried out day and night. In cases in which there was no contra-indication to its use a pre-operative test dose was given and the post-operative dosage calculated from it.

The operations carried out in 62 cases were as follows:

(1) Emergency operations carried out before full development of the collateral circulation:	(3) Operations on main vessels:
Direct ligation and division	Direct ligation and division
Arterial suture	Arterial suture
Proximal ligation	Aneurysmorrhaphy
	Ligation of fistula
	Ligation of neck of sac
23	25
(2) Operations on minor vessels (those whose ligation is usually safe):	
Excision	9
Quadruple ligation	3
Arterial suture	1
Aneurysmorrhaphy	1
	14

CASE I.—Sgt. I. S., aged 32, sustained a large wound of the popliteal fossa with severe external bleeding which required the application of a tourniquet for its control. The tourniquet was loosened at intervals and, ten hours after wounding, four pints of blood were transfused and the wound was excised. As the surgeon could feel the artery pulsating it was not explored. Eight hours later there was another brisk hæmorrhage which could only be arrested by the application of a tourniquet; two pints of blood were transfused, the wound was inspected and a superficial vein was ligated. Three days later the wound, which measured 7 by $4\frac{1}{2}$ in., was closed by suture. Five days after this operation there was another brisk hæmorrhage but this had stopped when he reached the theatre and two days later a superficial hæmatoma was evacuated without incident. On the fourteenth day after wounding, the patient noted throbbing and pulsation behind his knee. On his admission to the vascular centre there was a large varicose aneurysm of the popliteal vessels but his leg was not affected by ischæmia (fig. 1).

CASE II.—Cpl. R. M., aged 34, was wounded on a commando raid and could not be evacuated to the Italian mainland for thirty-six hours. He was admitted in a routine convoy forty-eight hours after wounding with through-and-through wounds of the thigh. The femoral artery was contused but not thrombosed and a musculo-fascial barrier was formed over it. A delayed traumatic aneurysm resulted and was treated at a later date with success and the limb was unaffected by ischæmic changes.

Only two cases but they serve to show the practical nature of the method. They also emphasize the need for retaining such cases under constant supervision and delaying their evacuation until the wounds have healed and the danger of further bleeding is over.

The results of primary ligation quoted do not take into account the severity of the associated soft tissue wounds. Arterial wounds fall into two main classes:

(1) *Those associated with large soft tissue wounds and severe external hæmorrhage.*—There is often severe damage to the potential collateral vessels. Such cases demand urgent surgical treatment which, in view of the almost inevitable laceration of the vessel wall, will result in ligation unless some means of restoring the circulation such as a type of Tuffier's tube or Blakemore's vein graft is employed. Restoration of the circulation in a limb whose blood flow has been interrupted for a considerable time leads to the rapid absorption of the products of disordered metabolism from it and may endanger the life of the patient. Further work is required before such methods can be brought into general use and until then the need for amputation following primary ligation in such cases should not be regarded as failure but as the price some patients have to pay for life-saving surgery.

(2) *Arterial wounds associated with trivial wounds of entry, with through-and-through wounds or occurring in multiple peppering with small fragments.*—This type is characterized by bleeding into the tissues and the clinical recognition of the arterial wound is of the utmost importance. The benefits of full wound excision can only be secured at the expense of the abrupt interruption of the blood flow, for ligation will be necessary in most cases. Despite the arterial injury there is always a flow of blood through the vessel and it is often sufficient for the peripheral pulses to be felt. All such wounds should be auscultated: the presence of local swelling and a systolic murmur are indicative of arterial

TABLE II.—78 CASES OF TRAUMATIC ANEURYSM.

Artery	No. of cases	False aneurysm	Aneurysmal varix	Varicose aneurysm	Primary Surgery		Wounds		Onset		Severe primary hæmorrhage	Operation
					Yes	No	Maj.	Min.	Immed.	Delay		
Ext. iliac	1	1	0	0	0	1	0	1	1	0	0	1
Femoral	10	4	4	2	2	8	1	9	8	2	3	3
Branches	3	2	1	0	1	2	0	3	3	0	4	13
Popliteal	13	2	8	3	3	10	1	12	11	0	1	1
Ant. tib.	1	1	0	0	1	0	1	0	1	0	2	0
Post. tib.	10	4	5	1	4	6	2	8	10	0	0	1
Subclav.	1	1	0	0	0	1	0	1	1	0	0	8
Axillary	10	4	5	1	0	10	0	10	7	3	4	5
Brachial	6	5	1	0	1	5	2	4	6	0	1	1
Branches	1	1	0	0	0	1	0	1	1	0	1	2
Radial	2	2	0	0	0	1	1	1	2	0	1	1
Ulnar	1	0	1	0	1	0	1	0	1	0	1	4
Sup. temp.	4	1	0	0	0	4	0	4	4	0	0	1
Ext. max.	1	1	0	0	0	1	0	1	1	0	0	1
C. carotid	3	2	1	0	0	3	0	3	3	0	0	1
E. carotid	3	3	0	0	0	3	0	3	3	0	0	3
I. carotid	3	0	3	0	0	3	0	3	3	0	0	1
? artery	5	—	—	—	0	5	0	5	4	1	0	—
Totals	78	37	29	7	14	64	9	69	69	9	16	62

wounding and operation should be delayed until the collateral circulation has become established in the absence of definite indications for earlier intervention. In the absence of local swelling and murmur failure to feel the peripheral pulses indicates complete division of the artery, contusion followed by thrombosis or traumatic arterial spasm and only exploration can establish the diagnosis.

Table II gives the details of the 78 cases of arterial injury of this type admitted to the Field Centre. Spontaneous cure resulted in two cases: (1) An aneurysmal varix of the superficial femoral artery, and (2) a small false aneurysm of the common carotid artery.

It is of interest to note that arterial suture was only possible in three of the emergency cases, an experience directly contrary to that of those who advocate early operation and repair.

Dissection was most difficult three to four weeks after wounding and was always more difficult in the larger lesions because of the increased fibrosis. In arterial and varicose aneurysms the false sac was opened and further dissection was carried out from within. Portions of the sac wall were never used to repair the vessel although in some cases after lateral suture of the arterial opening the suture line was reinforced by bringing the sac wall together over it. No attempt was made to remove the sac wall when important structures were incorporated in it and in cases in which its removal seemed likely to damage collateral vessels. Arterial branches entering the aneurysm were occluded by suture from within the sac. The companion vein was not ligated unless it was so damaged that its ligation could not be avoided.

Lumbar ganglionectomy was employed in one case in which the common iliac artery had to be ligated but apart from this case and a case of posterior tibial aneurysmal varix admitted after sympathectomy had been performed, sympathectomy was not carried out.

The control of hæmorrhage at operation.—A tourniquet was employed in arterial and varicose aneurysms but its use was given up in aneurysmal varices after failure to cure a posterior tibial fistula. When the site of the lesion precluded the use of a tourniquet the artery was exposed and temporarily secured above the lesion, and in all cases in which hæmorrhage was liable to be considerable an intravenous infusion was begun before operation in order that transfusion could be started immediately when required. Fresh blood was always used.

The results of treatment.—In the 62 operations there was one death following ligation of the common iliac artery just proximal to a huge lesion of the external iliac artery. The hæmatoma was pressing on the iliac vein. Following the operation the tension of the swelling was greatly reduced and twelve hours after operation the patient collapsed from overwhelming toxæmia probably from the absorption of metabolites from the limb.

In one axillary lesion operated on in emergency in which ischæmic changes were already present these were increased and gangrene of two digits occurred. Recurrence followed three weeks after operation in the case in which the fistula was ligated.

In the remaining cases there were no complications and secondary hæmorrhage after operation did not occur. In the suture operations the peripheral pulses were never lost whereas following direct ligation, even as long as two years after wounding, they were always absent for some days after operation. In three cases in which arteriography was carried out some eight weeks after arterial suture the arteries were shown to be patent and there was no sign of the development of a collateral circulation. In one of these cases the arteriogram showed a dilatation like a plumber's wiped joint at the site of the transvenous suture although this gave no signs on clinical examination (fig. 5).

A military surgeon can of necessity quote only immediate results and the correctness or otherwise of our approach to the problem can only be assessed by a long term follow up. It is to be hoped that this may yet prove possible at least in the British cases.

From the work of the special centre the following conclusions seem justifiable.

- (1) The initial treatment of arterial wounds associated with minor soft tissue wounds should be conservative.
- (2) Wounds in the vicinity of large vessels should always be auscultated before primary surgery is carried out.
- (3) Operation should be delayed until the collateral circulation is fully established in the absence of definite indications for earlier intervention.
- (4) The nature of the operation to be carried out can only be decided when the exact pathology has been displayed and assessed.
- (5) In arterial and varicose aneurysms a tourniquet should be employed. If this be impossible the proximal artery should be controlled provisionally as the first step in the operation and arrangements made for the immediate giving of blood.
- (6) The care of the potentially ischæmic limb is of the utmost importance and reflex vasodilatation is of definite value.
- (7) The blood volume should be restored to normal as soon as hæmorrhage is fully controlled.

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FIG. 1.

FIG. 1.—Varicose aneurysm of popliteal artery, Case 1.

FIG. 2.—Aneurysmal varix of posterior tibial artery accurately localized by arteriography.

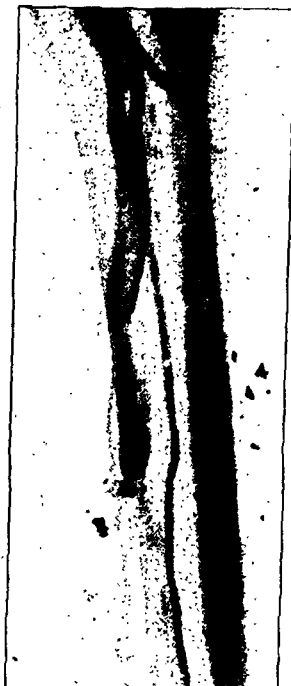


FIG. 2.

FIG. 3.—Small fistula of femoral artery and vein.

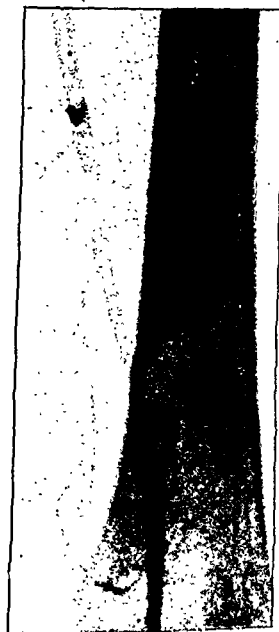


FIG. 3.

FIG. 4.—Gross dilatation of vein faintly outlined in aneurysmal varix of two years' duration. The arteriogram is of no value in establishing the exact site of the fistula in such cases.

FIG. 5.—Arteriogram taken eight weeks after transvenous suture of large fistula of popliteal artery and vein. The dilatation caused no symptoms or signs.



FIG. 4.

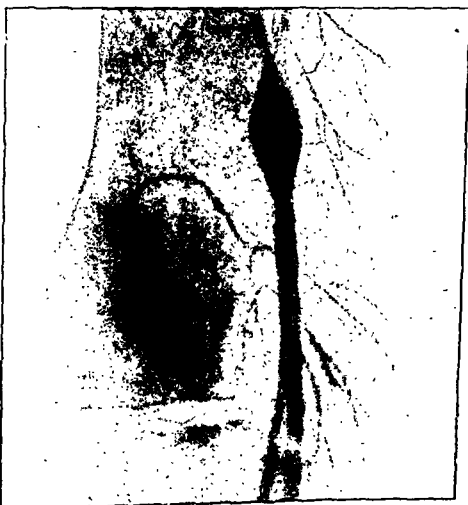


FIG. 5.

Arterial hæmatomas.—These were treated by ligature proximal and distal to the wounded point, with the addition of endo-aneurysmorrhaphy if any branch opened into the sac. If the sac dissected easily, as a general rule it was removed, but we had no hesitation in leaving the sac if it appeared possible that the dissection would risk collateral vessels. On one or two occasions we were chagrined to find that the cause of a lesion, which we had believed to be an injury to a peripheral nerve, was the existence of an arterial hæmatoma; for example in a case in which a false aneurysm of the thoracic axis had formed between the two heads of the median nerve. I believe it to be important that the ligatures should be placed as close as possible to the injured segment, and I do not agree with Holman (1944) that the proximal ligature should be placed just distal to the largest visible collateral. In our experience when an artery is cleanly divided between ligatures, the proximal clot is short and there seems no reason to doubt that branches too small to be seen at operation may subsequently enlarge to provide a proportion of the collateral circulation.

We have been specially interested in arterial aneurysms in the neck. On one occasion we had to deal with an aneurysm at the origin of the external carotid in which the foreign body had entered from the opposite side and had traversed the pharynx. The problem of access to more proximal aneurysms has not always been easy to solve. In one case in which a very large aneurysm having its origin in a wound of the third part of the subclavian artery extended into the superior mediastinum, the inner end of the clavicle and the upper part of the sternum were removed piecemeal subperiosteally, and we were glad to find that after this rather mutilating procedure function was very little impaired. In dealing with aneurysms of the common carotid artery for which ligature was likely, we have first performed a sympathectomy on the opposite side, and after seven days treated the aneurysm and done a sympathectomy on the same side in order to provide immediate maximal dilatation of collateral channels. In ligating the left common carotid artery at its origin from the aorta, a technical point of some importance is to ensure, by temporary occlusion of the vessel and palpation of the radial pulse, that one is not dealing with a left innominate artery.

Arteriovenous aneurysms.—The side-effects of these are well known. The earliest date at which we have detected cardiac enlargement is two months after injury. That the degree of cardiac enlargement depends on the size of the communication is shown quite well in a case in which two fistulæ were present. After dealing with the one between the superficial femoral artery and vein, the cardiac size diminished. We found, however, that a thrill and murmur still persisted, and six months after the first operation the heart had begun to enlarge again. At a second operation, a fistula between the profunda and the femoral vein was repaired.

With regard to the Branham phenomenon, my colleague Mr. Maybury communicated to me the acute clinical observation that while the diminution in pulse-rate followed immediately on the obliteration of the fistula, the return to the previous rate was a more gradual process, and this we verified by making a combined sound track and electrocardiogram in a patient who had a fistula between the medial circumflex artery and the profunda vein. Many of these patients show a relative polycythæmia as well as an increased blood volume, and in many the hæmoglobin content of the individual corpuscle is increased.

With regard to treatment, we have noticed spontaneous healing in one case in which a fistula had existed between the brachial artery and vein. Like other workers, we have seldom found it possible to carry out reparative surgery.

We have had a number of interesting anatomical types. In one case two fistulæ were present close to each other between the popliteal artery and vein. In a second case, which I have recorded (1945), both the common carotid and vertebral arteries contributed to the fistula. Ligation of both these vessels in a man of 43 was not followed by any untoward effect. In a third, a revolver bullet had completely divided the common carotid artery, and nine months afterwards at operation we found the distal end thrombosed while the proximal end communicated through a sac with a large opening in the internal jugular vein, thus giving rise to what was at least a partial reversal of the cerebral circulation as evidenced by unilateral swelling of the face and conjunctival venous stasis. This patient did well after operation.

Like other workers, we have had a patient with an arteriovenous aneurysm who did not know that he had been wounded. In none of our cases of arteriovenous aneurysm have we been able to detect any further nutritional change, either superficial or deep, after treatment by quadruple ligation and excision.

Mr. A. M. Boyd: My experience of vascular injuries is limited to those cases referred to a Base Hospital in Egypt between October 1942 and October 1945. Altogether 28 aneurysms were treated. A few recent injuries to blood-vessels from local accidents were seen. There were a few cases of secondary hæmorrhage. Altogether 41 main vessels were ligated for one reason or another.

Ligature of the main artery of a limb carries with it a considerable risk of gangrene. Sir George Makins collected a series in World War I in which the primary artery had been ligated and the fate of the limb left to the collateral blood flow.

The percentage of cases complicated by gangrene according to arteries involved were as follows: Subclavian 25%; axillary 16.6%; brachial 23%; femoral 25%; popliteal 41.6%.

Apart from frank gangrene depleted blood flow leads to ischæmic necrosis of muscle and fibrosis, wasting of muscles and nerve palsies. Even if these grosser manifestations are not seen inadequate blood supply to the muscles is revealed in the lower extremities by intermittent claudication. The fate of the limb after ligature of a main artery depends upon the collateral circulation. Every effort must be made to expand it quickly and blood-pressure must be kept up. The limb should be kept below the level of the heart by blocks under the head of the bed.

The limb should be kept cool to reduce metabolism and the rest of the body warm to aid sympathetic release.

The quickest method of dilating the collateral circulation is by sympathectomy. It has been practised in America for many years. Gage of New Orleans has carried out sympathetic block in all cases of traumatic injuries to blood-vessels and in operations upon aneurysms since 1930 without the occurrence of a single case of gangrene. Doubt has been cast upon the efficacy of this procedure by theoretical considerations. It has been stated that experimental stimulation of the sympathetic leads to vasoconstriction in the artery but increased blood flow to the muscles. Blocking the sympathetic would therefore reduce the flow to muscle.

Theis, however, has shown convincingly by animal experiment that sympathectomy increases the total inflow to a limb and also increases the collateral circulation after ligature of the main vessel.

Barcroft has recently shown that there are vasoconstrictor fibres in the muscles of man. Clinically it is well known that sympathectomy will improve intermittent claudication proving that the blood supply to the calf muscles has been improved.

I have ligated 41 main vessels. In 40 of them a sympathectomy was carried out either at the time of ligature or a fortnight before. Most of them were not simple ligations but extensive excisions of long segments of artery. In this series there was one example of gangrene following an excision of an arteriovenous aneurysm in Hunter's canal.

In one case of arteriovenous aneurysm of the first part of the right subclavian, sympathectomy was impracticable on account of dense adhesions round the apical pleura. Operation was followed by ischæmic necrosis of the forearm muscles.

In traumatic false aneurysm the artery was ligated on either side of the sac, the sac opened, clot turned out and subsidiary vessels ligated. As much of the sac wall that could be removed with safety was excised. A sympathectomy was carried out in each case.

Time of operation.—It is undoubtedly wise to wait three months before operation is undertaken, but in my experience it is seldom possible. In all but two cases, operation had to be carried out much earlier on account of bleeding, pain from pressure on nerves or infection.

In arteriovenous aneurysm quadruple ligature with excision of aneurysm when practicable, accompanied or preceded by a sympathectomy, was performed. There was one case of gangrene after an extensive excision of an aneurysm in Hunter's canal.

My experience leads me to believe that the safest method of ensuring an adequate collateral circulation is by releasing vasoconstriction by sympathectomy.

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Professor J. R. Learmonth: My part in this discussion is to give some account of the work at a vascular centre established in an Emergency Medical Service hospital by the Department of Health for Scotland. In general, we were not confronted with acute problems, except after D-day when we saw a few cases; the majority of our patients were seen some months after wounding.

(4) The way in which Professor Learmonth has applied to clinical surgery the observations of Sewall, Sandford, François Franck and later Stewart is of great interest. He has been able to produce vasodilatation in the affected limb by warming the opposite healthy limb, or even by warming the other limbs.

In this connexion, I wish to emphasize a point which seems to be of real interest. It is that simple obliteration of the main blood supply of the limb, whether by localized compression or by ligature, does not produce any vasoconstriction, but it does produce a considerable degree of vasodilatation comparable to that which is produced by lumbar ganglionectomy (figs. 1 and 2). This vasodilatation is constantly progressive and entails a fall of peripheral pressure which becomes more and more accentuated as the experiment proceeds; it is this which ultimately causes serious harm to the vitality of the tissues.

It is therefore obvious that any form of sympathectomy can only exaggerate the vasodilatation already produced by the arterial ligation. Its purpose would be to increase the proximal collateral circulation, but it produces at the same time a more marked vasodilatation.

Experiments have been made on dogs showing that disturbances in the peripheral circulation, following the ligature of the external iliac artery, disappear immediately after lumbar ganglionectomy; but they do not disprove our statement.

We have shown in different papers that the arterial circulation of the hind leg of a dog cannot be compared with that of a man, as long as the sacral aorta is functioning. We have further shown that in the normal dog the simple ligature of the external iliac artery very often does not produce any disturbances in the peripheral circulation, or, if it does, they are merely transitory. Circulation is restored without delay by way of the anastomoses, particularly by the main branches of the sacral aorta. To reproduce experimentally on a dog the conditions which exist in a man it is indispensable to begin by ligature of the sacral aorta. Many erroneous conclusions have been published, because their authors have not taken this fundamental point into account.

During the last war Oppel in Russia and Sir George Makins in this country recommended the ligation of the accompanying vein even when the lesion only involved the artery, and experience has shown that the results are thereby improved.

Fig. 3 shows that the peripheral pressure is higher on the side of the double ligature and the manometric readings even show respiratory and cardiac oscillations. How then does ligature of the corresponding vein produce its effects? Are they important and really useful?

Probably most workers in this field think that venous ligature simply produces a hydrostatic barrier limiting the flow of blood from the limb and thus raising the pressure in the capillary bed.

Our experimental work has shown us that the response to ligature or compression of the vein is extremely complex. It produces first a fall (fig. 4) in peripheral pressure which is rapidly succeeded by a rise. Arteriography has shown that this double reaction in reality is composed of two elements, vasoconstriction and vasodilatation, which do not simply follow each other but are coincident, associated and combined. Venous ligature produces a gross dilatation in the small vessels and a vasoconstriction in the main arteries and their large branches.

Besides the limitation of blood supply, the danger of obliteration of a main artery seems to lie in the general progressive diminution of peripheral pressure, which results from vasodilatation. Ligature or compression of the corresponding vein leads to a vasoconstriction which raises the peripheral pressure to a more normal level. Since this vasoconstriction only involves the large vessels, while the small vessels are dilated, the vitality of the tissues is markedly improved.

Of course, there is no need to use the ligature of the companion vein in all cases of ligature of the main artery. But there is a point of real importance in our statements, which is that the vasomotor reactions to the ligature or obliteration of the vein are quite independent of the nervous system, either central or peripheral. The patients may, therefore, benefit from these vasomotor reactions, even when one or all the nerves of the limb have been cut.

The main indication for ligature or compression of the companion vein will be particularly clear in cases of very extensive injuries, with combined arterial and nervous lesions, where other techniques for inducing peripheral vasodilatation are ineffective.

Methods of examination.—We have rarely used arteriography in the localization of arterial hæmatomas, and the method does not lend itself well to the identification of the site of an arteriovenous fistula. We have made considerable use of an observation, also indicated to me by Mr. Maybury, that the murmur in an arteriovenous fistula can be heard in the arm of the observer when his hand is placed over the region of the fistula. By using this method of "auscultation at a distance" with the index finger as the exploring digit, we have been able to localize the maximum point of intensity of a murmur with considerable accuracy. Finally, except in carotid lesions, we have not employed sympathectomy on more than one or two occasions as a preliminary to ligation of a large vessel. It has seemed to us that the collateral circulation after two or three months has always been adequate, and we have attempted to avoid any immediate post-operative risk by reflex vasodilatation combined with the administration of morphia which appears to have a decidedly beneficial effect in reducing vasoconstrictor tonus. Our practice has been to wrap the limb on which the operation has been done in a sterile towel without any constricting bandage, and to leave it at room temperature with the head of the bed slightly raised to interfere somewhat with the venous return. We are satisfied with the results of this procedure, except that it has become apparent that we ought more often to have realized the importance of preserving, if possible, the main venous channels, a refinement to which attention has recently been drawn by Professor Paterson Ross (1946).

Vascular tumours.—One matter which may not have come within the experience of surgeons in vascular centres in the theatre of war is the occasional development of a vascular tumour following injury. We have had several such cases, and in most, but not in all, a small cutaneous hæmangioma has previously been present, a circumstance which lends support to Reid's (1925) view that hæmangiomas in general represent areas in which the primitive arrangement of vessels has not completely developed into its permanent form. One example will suffice. A pilot officer knocked his arm on the wing of his aeroplane, over the site of a small nævus, and eighteen months afterwards this area was the site of a large pulsating tangle of vessels fed by three large trunks containing arterial blood. The tumour involved the skin and sent communications to the intramuscular clefts. It lent itself to excision with a satisfactory result. I mention this type of case because I believe that other examples will turn up from time to time in the post-war period.

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Professor F. Albert (Liège): My own clinical experience dates from the last war, since when I have been continuously interested in all aspects of the surgery and pathology of vascular lesions, the treatment of which has benefited in no small degree by the general progress brought about by the use of sulphonamides, heparin, and the discovery of penicillin.

It has been known for many years that the obliteration of a large artery is followed by vasomotor disturbances of critical importance. On the Continent at least there is a tendency to regard these reactions as being purely vasoconstrictor in origin, which therefore demand therapeutic measures in order to produce vasodilatation.

In the past there has been a general consensus of opinion that all obliterative arterial lesions, which are accompanied by irritation of the vessel wall, directly cause vasoconstrictor reflexes. This view has particular reference to trauma of the arteries which is followed by thrombosis, to arterial embolism and spasm. It even includes venous thrombosis, especially when accompanied by phlebitis.

To deal with these vasoconstrictive phenomena the most useful means at our disposal have been:

- (1) Resection of the thrombosed segment or removal of the embolus, which, if done early, also prevents extension of the thrombosis to the collateral vessels.
- (2) Infiltration of the appropriate sympathetic chain with novocain when the disease is acute, or, when the patient's condition permits, resection of the sympathetic chain in less acute or chronic lesions.
- (3) More recently peri-arterial infiltration with novocain, or even proximal intra-arterial injection of novocain has been used; and the latter is specially useful when obliteration is incomplete.

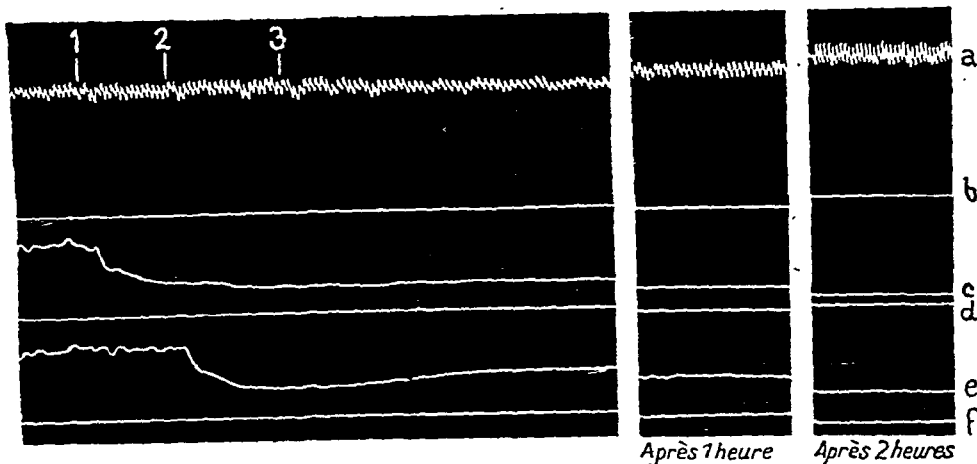


FIG. 3.—Dog weighing 28 lb. given 1.75 gramme chloralose intravenously. Ligation on the middle sacral artery. At (1) the left common iliac artery was ligated, and at (2) the right common iliac. At (3) the right common iliac vein was tied.

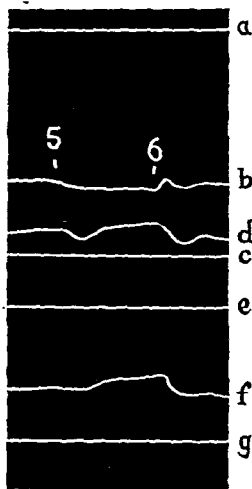
On the left side the peripheral pressure falls progressively for the whole of the experiment. On the right side it rises again rapidly after ligation of the vein and maintains a level much higher than the left; moreover the cardiac and respiratory oscillations reappear.

(From "Les oblitérations artérielles. Etude physio-pathologique", by F. Albert, in *Lyon chirurgical*, 29, 619.)

FIG. 4.—(a). Time in seconds. (b) Pressure in central end of axillary artery. (c) Base line. (d) Pressure in peripheral end of right femoral artery. (e) Base line. (f) Pressure in peripheral end of left femoral artery. (g) Base line.

Between (5) and (6) the vena cava was occluded. Note the difference in vasomotor response between the right and the left. The right limb at first showed much more marked vasoconstriction than the left.

(From "A propos des ligatures veineuses. Etude expérimentale des réactions vaso-motrices périphériques", by F. Albert, *Lyon chirurgical*, 29, 273.)



Mr. B. C. Maybury gave the results of a preliminary "follow-up" of 34 patients suffering from traumatic false aneurysm and arteriovenous fistula treated at Park Prewett E.M.S. Hospital, Basingstoke. The arteries involved were internal and external carotid 1 case, first part axillary 2 cases, third part axillary 4, brachial 5, radial 1, common femoral 1, superficial femoral 7, profunda femoris 2, popliteal 9, posterior tibial 1, transversalis colli 1. To ensure an adequate collateral circulation, the general policy had been to wait two to three months in the upper extremity and three to four months in the lower before operation was undertaken, though sometimes the time of operation had to be advanced for the well-known indications of rapid increase in the size of the sac, hæmorrhage, pain, &c. Sympathectomy had not been performed on any patient, but the corresponding vein had been tied in all except one, even when a suture operation had been performed. Two patients had not been subjected to operation, one with an aneurysmal varix of the transversalis colli causing no symptoms, and the other with a popliteal aneurysm who was subjected to an injection of the superficial femoral with pyelectan for an arteriogram; as a direct result the femoral and popliteal arteries and the aneurysm thrombosed; he suffered a serious ischæmic myositis of the anterior tibial group but was able to walk.

In the whole series of 32 patients operated on neither gangrene nor ischæmic myositis had occurred and there had been no mortality. The absence of the latter was largely due to there having been no cases of aneurysms or fistulae at the root of the neck and

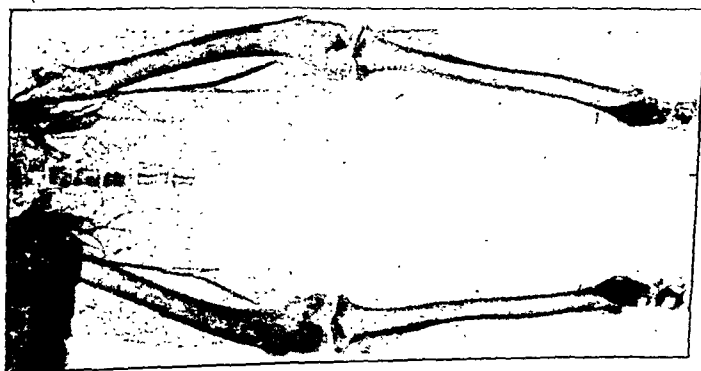


FIG. 1.—Normal arteriogram with some slight vasoconstriction.

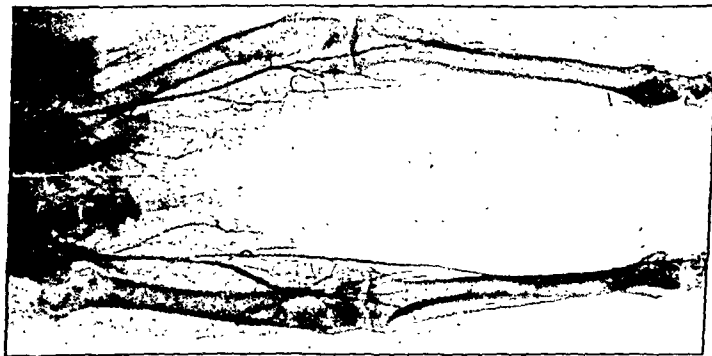


FIG. 2.—Same animal after left lumbar ganglionectomy and compression of the right common iliac artery for six minutes.

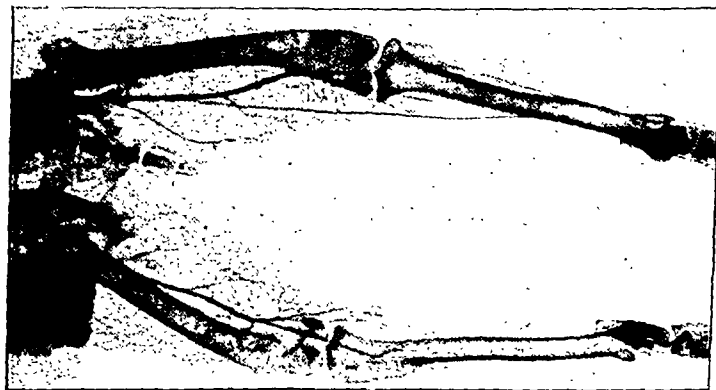


FIG. 3.—Arteriogram taken after six minutes' compression of the right common iliac vein. There is vasoconstriction of the large vessels and dilation of all the small muscular branches.



FIG. 4.—The same preparation, larger size, showing details of the small vessels.

(These arteriograms are copied from "Les compressions vasculaires, Etude artériographique," by F. Albert, in the *Revue belge des Sciences médicales*, Vol. 9, No. 3.)

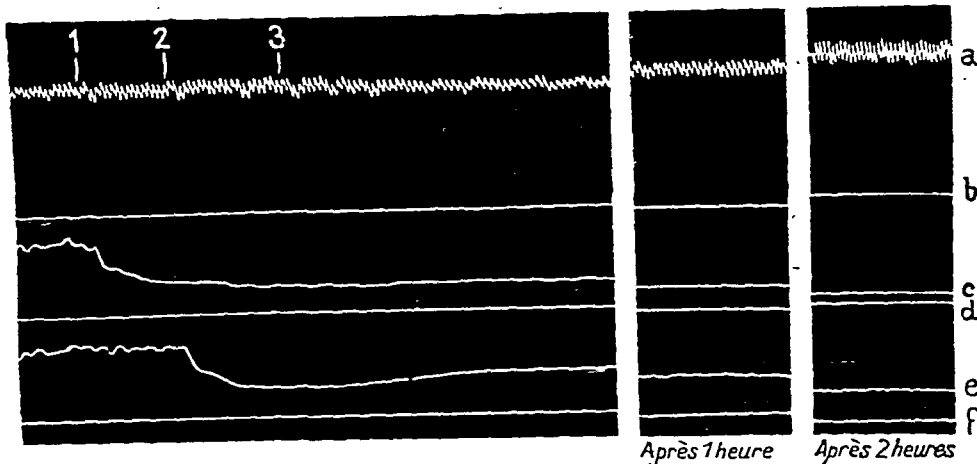


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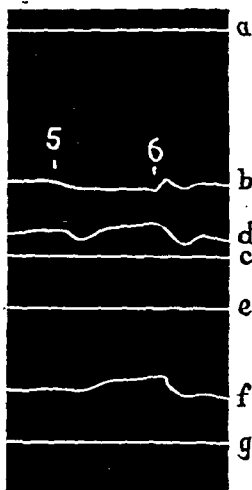
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only one of the internal carotid; the latter, an arteriovenous aneurysm of the internal and external carotid and jugular vein, treated by immediate proximal ligation of both arteries and a remote distal ligation of the external carotid (with ligation of the jugular vein) had been converted into an aneurysmal varix and, although the murmur was still present, it was less and not audible to the patient seven months later. The remaining 31 patients operated on had been cured of their arterial lesions.

Immediate proximal and distal ligation had been performed on 25 and arterial suture on 6. The latter figure was disappointing but as excuse there were only 6 aneurysmal varices, the remainder being made up of 17 varicose aneurysms and 11 false aneurysms and arterial hæmatomata. There is no doubt it is much easier to suture the hole in an aneurysmal varix than in either of the other two lesions; the hole is usually smaller and the absence of early extravasation of blood ensures the absence of a later fibrosis. Operating on an arteriovenous aneurysm meant for him at any rate two or three hours of "toil, blood and sweat" and he was only too thankful at the end of that time to get ligatures applied. Of the 6 suture operations, 3 were completely successful, 1 partially successful (thrombosis occurred ten days later) and 2 were failures as regards patency of the vessel.

The period between the operation and the "follow-up" varied from three weeks to sixteen months, but was mainly about nine months. In all cases where ligation had been performed the systolic and diastolic pressures were well below those of the opposite side, the former usually 20 to 40 mm.Hg and the latter 10 to 20 mm.Hg.

In the case of the upper extremity the frequency of associated nerve lesions often prevented an accurate estimation of the disability due to the arterial ligation, but in the case of the lower extremity the arterial lesion is more often uncomplicated. Several patients complained of intermittent claudication after walking two or three miles. In a few there was very slight œdema of the leg detected only by picking up a fold of skin and comparing its thickness with that of the opposite side. In several there was $\frac{1}{4}$ in. to $\frac{1}{2}$ in. increase in the girth of the leg at calf level. He was rather inclined to explain these two changes as being due to a local "starvation œdema" rather than to the vein having been tied. It was of interest to note that two of the three patients who had had successful suture operations showed no œdema although the vein had been tied, while the third, although showing slight œdema, had had a fractured femur. Only one patient showed any evidence of superficial varicose veins.

It was clear that all these patients have useful limbs which, however, have a lower circulatory reserve and will not stand up to heavy and prolonged work.

His object in giving these results was to provide a series of cases in which sympathectomy had not been performed, but in which the vein had been tied, for comparison with a similar series in which sympathectomy had been done and the vein not tied, which he hoped someone else would produce.

He wished to thank his colleagues, Messrs. White, Innes and Sames, and particularly Mr. Denys Williams, who had been responsible for the records.

He was very interested in Mr. Mason Brown's report of cases in which he had made use of a musculo-fascial barrier in the early treatment of a partial division of an artery. He had used this procedure himself in the last war and it was also of value in the lesion known as *contusion* without thrombosis when a portion of the arterial wall was apt to give way up to the 21st day: the barrier converted what would otherwise be a secondary hæmorrhage into an arterial hæmatoma, thus affording time for some collateral circulation before ligation.

He had been impressed by the term "parasitic circulation" first used by Holman to describe that part of the circulation which flowed from the heart through an arteriovenous fistula back to the heart. It covered, but did not explain, the known facts, viz. the cardiac enlargement, the arterial enlargement on the proximal side, the enlarged vein and the increased blood volume. The term deserved to be more widely known and used.

JOINT DISCUSSION No. 2

Section of Medicine with Section of Surgery

Chairman—T. IZOD BENNETT, M.D., F.R.C.P.

(President of the Section of Medicine)

[January 29, 1946]

DIAGNOSIS AND TREATMENT OF CHRONIC CHOLECYSTITIS

Dr. Maurice Shaw: From the point of view of treatment it is useful to regard chronic cholecystitis as occurring in two main forms, one an interstitial inflammation involving the wall of the gall-bladder and the other a catarrhal condition in which, at first at any rate, the walls are not greatly, if at all, involved. In the former type stone formation is common and gross disturbance of function can frequently be demonstrated by cholecystography; in the latter radiological examination may be completely negative.

An interesting point in the symptomatology of patients with gall-bladder disease is the gastric flatulence. This is almost certainly not the result of any actual excess of gas in the stomach as such patients are not aerophagists. The true explanation may be that the sensation of fullness is the result of an increase in gastric tonus causing the normal air content of the stomach to exert an undue pressure on its walls. The high intra-gastric tension which results is, of course, relieved by the eructation of some of this gas.

Probably one of the most controversial points in the diagnosis of cholecystitis is the question whether the absence of positive radiological signs can be taken to exclude disease of the organ. It is still the custom of some radiologists to report that the gall-bladder is normal but I cannot believe that it is possible to be sure that a gall-bladder is really radiologically normal by merely inspecting the shadow cast by an opaque material in its interior. We should not expect X-rays to show the presence of a pyelitis after intravenous pyelography and the analogy between this condition and what I have called catarrhal cholecystitis is a close one. It is in these cases that the clinical signs combined with such ancillary methods as duodenal intubation must be relied upon to provide the diagnosis but it must be confessed that it is impossible to attain anything like certainty in a fairly large proportion of cases. In these the therapeutic test must often be applied. When treatment has failed to alleviate the patient's symptoms the decision may have to be made as to surgical treatment even in the absence of demonstrable abnormality. It is in such cases that surgeons are often reluctant to operate but I do not think there can be any doubt that many such patients respond well to surgical treatment although their selection must always be a matter of great difficulty and, until more precise diagnostic methods have been introduced, we shall continue to experience disappointments.

In the case of interstitial cholecystitis it is hardly ever possible to achieve much by medical treatment but there does seem a possibility that in the future a combination of

only one of the internal carotid; the latter, an arteriovenous aneurysm of the internal and external carotid and jugular vein, treated by immediate proximal ligation of both arteries and a remote distal ligation of the external carotid (with ligation of the jugular vein) had been converted into an aneurysmal varix and, although the murmur was still present, it was less and not audible to the patient seven months later. The remaining 31 patients operated on had been cured of their arterial lesions.

Immediate proximal and distal ligation had been performed on 25 and arterial suture on 6. The latter figure was disappointing but as excuse there were only 6 aneurysmal varices, the remainder being made up of 17 varicose aneurysms and 11 false aneurysms and arterial hæmatomata. There is no doubt it is much easier to suture the hole in an aneurysmal varix than in either of the other two lesions; the hole is usually smaller and the absence of early extravasation of blood ensures the absence of a later fibrosis. Operating on an arteriovenous aneurysm meant for him at any rate two or three hours of "toil, blood and sweat" and he was only too thankful at the end of that time to get ligatures applied. Of the 6 suture operations, 3 were completely successful, 1 partially successful (thrombosis occurred ten days later) and 2 were failures as regards patency of the vessel.

The period between the operation and the "follow-up" varied from three weeks to sixteen months, but was mainly about nine months. In all cases where ligation had been performed the systolic and diastolic pressures were well below those of the opposite side, the former usually 20 to 40 mm.Hg and the latter 10 to 20 mm.Hg.

In the case of the upper extremity the frequency of associated nerve lesions often prevented an accurate estimation of the disability due to the arterial ligation, but in the case of the lower extremity the arterial lesion is more often uncomplicated. Several patients complained of intermittent claudication after walking two or three miles. In a few there was very slight œdema of the leg detected only by picking up a fold of skin and comparing its thickness with that of the opposite side. In several there was $\frac{1}{4}$ in. to $\frac{1}{2}$ in. increase in the girth of the leg at calf level. He was rather inclined to explain these two changes as being due to a local "starvation œdema" rather than to the vein having been tied. It was of interest to note that two of the three patients who had had successful suture operations showed no œdema although the vein had been tied, while the third, although showing slight œdema, had had a fractured femur. Only one patient showed any evidence of superficial varicose veins.

It was clear that all these patients have useful limbs which, however, have a lower circulatory reserve and will not stand up to heavy and prolonged work.

His object in giving these results was to provide a series of cases in which sympathectomy had not been performed, but in which the vein had been tied, for comparison with a similar series in which sympathectomy had been done and the vein not tied, which he hoped someone else would produce.

He wished to thank his colleagues, Messrs. White, Innes and Sames, and particularly Mr. Denys Williams, who had been responsible for the records.

He was very interested in Mr. Mason Brown's report of cases in which he had made use of a musculo-fascial barrier in the early treatment of a partial division of an artery. He had used this procedure himself in the last war and it was also of value in the lesion known as contusion without thrombosis when a portion of the arterial wall was apt to give way up to the 21st day: the barrier converted what would otherwise be a secondary hæmorrhage into an arterial hæmatoma, thus affording time for some collateral circulation before ligation.

He had been impressed by the term "parasitic circulation" first used by Holman to describe that part of the circulation which flowed from the heart through an arterio-venous fistula back to the heart. It covered, but did not explain, the known facts, viz. the cardiac enlargement, the arterial enlargement on the proximal side, the enlarged vein and the increased blood volume. The term deserved to be more widely known and used.

iodophenolphthalein, now known as iodophthalein B.P. Its isomeride sodium phenol tetra-iodophthalein has not been manufactured in this country and it has scarcely been used here. Recently, an entirely new contrast medium, hydroxy-iodophenyl-phenyl-propionic acid, has been produced. The Medical Research Council in 1942 announced that the name of Pheniodol B.P. had been adopted for this compound, originally manufactured abroad. It is taken by mouth only. It disturbs the patient less than the phthalein compounds. The density of the shadow and the results are usually as good as those following the intravenous injection of iodophthalein. No better results have been obtained by the more complicated routines, often used because of the relative inefficiency of the so-called "dyes" when taken by mouth. It is usual to give the compound at night, and to make the examination next morning, the patient fasting.

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(2) Though otherwise radiologically normal, it may empty slowly, whether it contracts or not. Even twenty-four hours after the fatty meal, much opaque material is often seen. Since using pheniodol, one has noticed this delayed emptying more frequently, possibly because of the greater density of the shadow. The gall-bladder is seen often, though not always, to shrink in size when gall-stones are present; even though afterwards the pathological report reads that the walls are thickened and fibrosed.

Does the emptying rate, and perhaps also the contractibility, mean more than the rapid or slow emptying rate of the otherwise normal stomach. Like the latter, it may vary in speed in the same person at different examinations. Is it more than a visible manifestation of an inward and mental state? a psychosomatic condition? In discussing the emptying rate and the contractibility of the gall-bladder, it seems curious that no reference is ever made to the possibility that the liver has made some more bile, and that this is entering and filling the gall-bladder.

(3) When the gall-bladder fails to fill with and to concentrate the opaque medium, four things may have happened:

(a) The medium may never have been extracted from the blood: so much of the liver must be destroyed before bile is no longer excreted, that in the clinical picture, attention is not likely to be focused on the gall-bladder.

(b) The medium, like the bile, may never have been able to leave the liver, or at any rate to reach the common bile duct and jaundice results. As a general rule, cholecystography is obviously contra-indicated in jaundice, though if carried out in some cases of infective hepatitis, a poor filling of a small gall-bladder may be seen. Again, clinically, it is the liver and not the gall-bladder that beckons.

(c) The iodine-containing bile may have been prevented from reaching the gall-bladder: in most cases by a calculus in the neck or the cystic duct itself, but adhesions, perhaps from a duodenal ulcer, or other causes may obstruct the duct to such an extent that "no filling" is reported, even though the gall-bladder itself is normal.

(d) Finally the mucous membrane of the gall-bladder may have lost its power to concentrate the bile, whether gall-stones are present or not, as in true cholecystitis.

A sub-division of this group is that in which the density of the shadow is less than normal—? a temporary or permanent but partial loss of function by the mucous membrane. The density may sometimes be greater, or less, at a second examination after a period of medical treatment. These are the cases which are so difficult to assess. If the shadow is below the average, has the mucous membrane partially lost its power to concentrate: (1) Because of a non-opaque calculus or other block which produces a partial stoppage and so a reduced entry of bile to the gall-bladder; (2) because the gall-bladder is unusually large and the same amount of opaque material spread over a broad area produces a lesser density; (3) because of inflammatory changes in the wall; (4) because of a temporary vasomotor or similar disturbance.

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The fallacies are: (1) Congenital anomalies.

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penicillin and sulphonamides may succeed in eradicating an infection which is too deep-seated to be affected by methods hitherto available.

The treatment, by medical means, of catarrhal cholecystitis can be considered under four headings: diet, drainage, disinfection and drugs. I have never seen any sound reason for withholding fats from patients with gall-bladder disease provided they can tolerate them—which, of course, is often not the case. The fat-free diet has come to be accepted from a misconception of the mechanism of cholesterol metabolism. There is no evidence, as far as I am aware, that the level of the blood cholesterol materially affects the cholesterol content of the bile nor, indeed, that the blood cholesterol can be significantly changed by high cholesterol feeding. Those conditions which are characterized by the highest blood cholesterol levels known to medicine, e.g. diabetes and nephrosis, are not associated with any particular tendency to the formation of gall-stones. It is true that certain patients spontaneously volunteer the information that they are intolerant of fats but close inquiry will often show that it is only certain types of fatty food which cause discomfort, particularly fried foods. Butter, eggs and cream are often surprisingly well tolerated. One of our main objects in treating an infected gall-bladder is free drainage and this can best be achieved by giving drugs and diet which stimulate emptying of the gall-bladder. For this purpose fats are especially useful and it has long been my own practice to encourage a diet rich in suitable fats to patients who are found to tolerate them well.

Of the drugs which promote drainage magnesium sulphate has the greatest reputation although the pharmacological evidence that this drug causes contraction of the gall-bladder is not entirely satisfactory. The therapeutic use of the duodenal tube has rather been abandoned in this country because it seems to be generally felt that the administration of magnesium sulphate by mouth is equally effective and causes less discomfort to the patient. In addition to the cholagogues, choleretic drugs such as decholin have a place in the treatment of gall-bladder disease by non-surgical biliary drainage.

For the purposes of disinfection the drugs which have been most widely used are the salicylates, hexamine and the sulphonamides. I have used hexamine and, judging by clinical results, with a fair degree of success but it is difficult to assess results without bacteriological control. It should be used in very large doses and stringent precaution must be taken to ensure that the urine is permanently alkaline for fear of damaging the kidneys. I have usually adopted the technique of giving a single large dose, as much as 200 grains, in the evening two hours after the last meal which must be taken reasonably early, say at 6 p.m. Thereafter nothing at all may be taken until a late breakfast the next morning. In this way a high concentration of the drug is maintained in the gall-bladder for a reasonably long time. Recent work has shown that the sulphonamides are excreted in the bile in therapeutically significant concentrations and their use is always worth while. The most useful drugs of this class are probably sulphathiazole and sulphadiazine.

Dr. G. T. Calthrop (*in absentia*, read by **Dr. J. W. D. Bull**): Cholecystitis is a disease of the gall-bladder, that is, of the walls of the gall-bladder. The gall-bladder and the bile are made up of chemical elements similar to those of the surrounding tissues. X-rays, therefore, do not differentiate them from their neighbours. It has been said that the gall-bladder can often be seen in plain films—perhaps because it contains bile of high calcium content. However this may be, it has been my misfortune that whenever I have identified the gall-bladder in the preliminary radiograph, the cholecystographs later showed that it was in an entirely different place!

When the gall-bladder contains some substance which in its composition has enough of an element of high atomic weight, that element opposes the passage of X-rays more than do the surrounding tissues, and so a shadow is produced on a film, just as it is by a barium meal. There are three occasions when this happens: (1) When there is a gall-stone containing calcium; (2) When the walls of the gall-bladder are calcified: the so-called porcelain gall-bladder; (3) Cholecystography.

Cholecystography is the adaptation of Rowntree and Abel's discovery that phenolphthalein was extracted from the blood by the liver and excreted in the bile.

The use of halogen compound, a derivative of phenolphthalein, was introduced by Graham and Cole in 1924, and the term Graham's test is often used as being synonymous with cholecystography. The tetra-chloro and the tetra-bromo derivatives were soon discarded in favour of the corresponding iodine compound, the di-sodium salt of tetra-

iodophenolphthalein, now known as iodophthalein B.P. Its isomeride sodium phenol tetra-iodophthalein has not been manufactured in this country and it has scarcely been used here. Recently, an entirely new contrast medium, hydroxy-iodophenyl-phenyl-propionic acid, has been produced. The Medical Research Council in 1942 announced that the name of Pheniodol B.P. had been adopted for this compound, originally manufactured abroad. It is taken by mouth only. It disturbs the patient less than the phthalein compounds. The density of the shadow and the results are usually as good as those following the intravenous injection of iodophthalein. No better results have been obtained by the more complicated routines, often used because of the relative inefficiency of the so-called "dyes" when taken by mouth. It is usual to give the compound at night, and to make the examination next morning, the patient fasting.

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to report its *absence* in the human. Knox, Mentzer, Schaeffer and Hirschbaum report in all on about 10,000 autopsies and found only 5 cases where the gall-bladder was congenitally absent. *Rudimentary* gall-bladders are equally rare. In one series of 10,000 examinations, 5 cases of *double* gall-bladder are reported. When two are present, disease may affect only the one.

These are obviously all very rare findings. When there are symptoms suggesting disease of the gall-bladder, the risk that congenital anomalies are producing misleading cholecystographs is extremely small.

(2) A gall-bladder which has failed to fill with and to concentrate the opaque medium may have done so because, so to speak, it is no longer there; cholecystography has been requested often after cholecystectomy. It is obviously impossible to fill a gall-bladder which has been removed! To request "cholecystography" because it is not certain whether the gall-bladder was removed, or whether it was only drained, and has perhaps recovered its function, is another matter.

(3) Improper preparation and poor radiographic technique can, and often do, mislead. It may be that the patient misunderstood the instructions or even that he has wilfully failed to take the iodophthalein or the pheniodol by mouth. The intravenous injection, providing it is intravenous, a painful and sad incident if it is not, will avoid this. The patient may have taken a large breakfast of bacon and eggs and so emptied his gall-bladder before the examination is made! A far more common cause of faulty interpretations is due to unsatisfactory technique: either the wrong dosage of the opaque medium, movement during the exposure, incorrect positioning or unsuitable radiographic factors. These can often be assessed, and if apparatus and electrical conditions are suitable, can be improved at a second examination. Overlying gas shadows are frequently a nuisance. Good technique will in most cases enable one to project them away from the gall-bladder. The same thing applies to the unabsorbed iodophthalein when taken by the oral route, but scarcely ever by the intravenous route or with pheniodol.

No reference has been made to cholesterosis or the strawberry gall-bladder. This is because I have not been able to convince myself that there are *any* radiological signs of its presence.

No attempt has been made to give statistics. It is found when inquiry is made afterwards, that in only a small proportion of abnormal cholecystographs is there a histological report or even a surgical finding! Figures therefore would be of no value. Clinicians who see the cases can perhaps speak with greater authority from their own experience.

To sum up:

(1) The gall-bladder may be radiologically normal in appearance and function. When the examination has been made *properly*, in what percentage of cases do the clinical, the surgical, and eventually the therapeutic findings, disagree with the radiological report?

(2) Proper technique having been used, when a gall-bladder fails to fill with and to concentrate the opaque medium, a pathological condition is practically always present, not necessarily in the gall-bladder, or its duct, though usually so. Since radiologically it is not possible to say whether the disease is outside the gall-bladder, due to one or more non-opaque gall-stones or to cholecystitis, there is obviously no direct radiological sign of cholecystitis.

(3) When there is only a poor filling and no gall-stones can be seen, care is needed. The clinical evidence must be very definite, otherwise it is better to check by a second examination; after an interval.

(4) The emptying rate of the gall-bladder varies. Has this any significance in the diagnosis of cholecystitis, or even in the diagnosis of any actual lesion?

Mr. A. J. Gardham: *Chronic cholecystitis without stones.*—Cases with a presumptive diagnosis of chronic cholecystitis without stones may be divided into two groups: (1) Those in whom disease of the biliary system is indicated by jaundice, and (2) those in whom it has been diagnosed on less certain grounds.

In Group 2 the clinical picture as I meet it is fairly typical; the patient is generally a woman, often of the type and habit traditionally associated with gall-stones and she

complains of pain which is variable in intensity; never of the severity of a true biliary colic and is situated, vaguely, in the right upper abdomen. She has no physical signs and brings with her X-ray plates which show either a normal gall-bladder, or one which concentrates poorly, or perhaps one which fails altogether to show on cholecystography. If the gall-bladder fails to show altogether I generally take it that I am dealing with a cystic duct which is blocked by a stone which is not visible on X-ray examination. My radiological colleague has referred to the possibility of the mucosa losing its power of concentration to such an extent that the gall-bladder fails to show altogether on cholecystography, even when there are no stones present. The only circumstances in which I have seen such cases are when gall-stones have been present and have escaped, either by means of a fistula, or by the normal passages; and provided that I am assured of the technical efficiency of the X-ray examination, I am prepared to take the evidence that there is no shadow on cholecystography to mean that a stone is or has been present.

The group of cases in which, on X-ray examination, the function is diminished or unimpaired makes a very different story. My experience of surgery in these cases is both limited and discouraging. I have removed a few such gall-bladders, always at the request of a physician; some of them have been normal to external examination, others have looked thick and inflamed. Sometimes the mucosa has been normal, sometimes it has been thick and sometimes it has been actually studded with cholesterin. The only thing which these cases have in common is that I have always regretted operating on them because the improvement in their health does not seem to me to be sufficient to compensate for the discomforts and risks of what is, after all, a major operation.

The only justification which I can see for operation in cases of this sort is that a timely operation for the removal of a gall-bladder which is not yet grossly diseased may prevent the formation of gall-stones and avoid the invalidism which results from the presence of stones in patients who are no longer in a fit condition to stand the operation of cholecystectomy. My impression is, although I cannot confirm it by statistics, that the patients who suffer from the symptoms generally attributed to cholecystitis without stones are of a younger age-group than those who come up with frank cholelithiasis.

If the theory of infection as a primary cause for gall-stones is correct, all the cases of frank gall-stones that we see must have a precalculus stage of cholecystitis lasting for years; yet in the majority of cases neither they nor their doctors have thought the symptoms sufficiently bothersome to merit the attention of a surgeon. So if a gall-bladder at this stage requires operation it is on the grounds of prognosis and not of symptoms. It is also worth while remembering that an inflammation of the gall-bladder, severe enough to lead to perforation into the duodenum, may be practically symptomless. I myself have seen two cases in which a fistula between the gall-bladder and the duodenum was discovered accidentally at an X-ray examination and I believe that it is the exception in cases of gall-stone obstruction of the small intestine to obtain a history of any symptoms suggestive of a severe and long-continued inflammation of the gall-bladder. Consideration of these facts leads me to the belief that cholecystitis without stones is not a good explanation for abdominal symptoms and that such symptoms are unlikely to be relieved by removal of a non-calculous gall-bladder. Even if the theory that gall-stones are infective in nature is not correct and that it is a metabolic error which leads to formation of the stones, it seems most unlikely that the gall-bladder could be the only organ affected by the metabolic change, and if it only shares with many other organs the effects of this change, the excuse for its extirpation unless stones are actually present and giving rise to symptoms is even slighter.

We may now consider the cases which present with a history of jaundice. These, in some ways, are more difficult because we know that disease of the biliary system is present. Most frequently the story is that of a case with an undoubted history of biliary colic and jaundice, without X-ray evidence of stones. I see quite a number of these cases, and I generally allow the patient to have two attacks before I advise operation. Operating on these indications I have found gall-bladders which are apparently normal, and when opened contain no stones, but I have also found gall-bladders which to external examination were normal, but on opening showed one or more tiny stones, ready to pass into the common duct. It is not at all easy for a surgeon to decide what action he will take in these circumstances. The easy thing for him to say is that however normal the gall-bladder looks, it may contain or at least have contained stones and that it should be removed. Unfortunately all surgeons know that a proportion of these cases continue to have similar attacks after removal of the gall-bladder, and they are a source of great anxiety to surgeons, because the question always arises of whether the operator may

possibly have overlooked a stone in the common duct. The problem before the surgeon is whether there is such a condition as dyskinesia of the biliary passages where owing to a failure of relaxation of the sphincter of Oddi the pressure in the common bile duct rises to the point where pain is produced, without there being any organic obstruction. Such a condition exists in the ureter and can be seen by cystoscopy, and is called cystic dilatation of the ureteric orifice. There is a considerable probability that some analogous condition does occur in the biliary passages, although we cannot see the ampulla of Vater, and personally I think it does, although it is rare. In any case the condition is one which merits the very serious attention of a surgeon who is dealing with a case where the history is that of attacks of biliary colic with jaundice and no stone can be demonstrated. The treatment of these cases is a technical surgical problem and I think it would be out of place to discuss it here; perhaps it can be summed up most adequately by saying that the more one has considered these possibilities, the less ready one is to remove a gall-bladder which is not obviously diseased.

Before concluding, I think it would be appropriate to mention the possibilities of peritoneoscopy. The gall-bladder is an organ which is almost visible on peritoneoscopy, unless it is abnormal and buried in adhesions, and although a normal appearance of the gall-bladder does not always exclude the possibility of calculi it may answer the question of whether an operation is necessary. I have found peritoneoscopy particularly useful in a type of case which seems to have become more frequent recently; that is a patient with very severe and persistent jaundice which had at first been regarded as an infective hepatitis, but has finally worn down the confidence of the physician to such an extent that he has called in the surgeon because he thinks he may be dealing with a stone in the common bile duct which is showing abnormal symptoms. Laparotomy in such cases is a very serious matter, and it may be possible by peritoneoscopy to establish that the gall-bladder is neither distended as it would be if there were a growth obstructing the common bile duct, nor inflamed as it would be if there were an obstruction caused by a stone. If, in fact, a normal gall-bladder can be seen in combination with a liver which is moderately enlarged and shows a greenish slaty appearance, it is fairly safe to say that the case is one of infective hepatitis.

A discussion followed in which the undermentioned took part: Professor B. Kopan, Dr. C. H. Atkinson, Professor B. O. C. Pribram, Dr. E. R. Cullinan, Dr. D. Gillespie.

Section of the History of Medicine

President—SIR ARTHUR MACNALT, K.C.B., M.D.

[October 3, 1945]

The Influence of Medical Poets on English Poetry

PRESIDENT'S ADDRESS

By Sir ARTHUR MACNALT, K.C.B., M.D.

This paper will be published in full in the June issue of the *Poetry Review*, the journal of the Poetry Society Incorporated.

[April 3, 1946]

Male Eunuchism Considered in the Light of the Historical Method

By A. P. CAWADIAS, O.B.E., M.D.

THE natural history of diseases, which is the science of medicine, is usually described by means of the didactic method, which consists in giving all the facts and conceptions accepted at the time of publication about the four chapters of this natural history, i.e. the ætiological, the symptomatological, the physiopathological and the therapeutic. This didactic method, although good as a rough guide in everyday practice, is insufficient for intimate understanding of the particular disease, and provides no basis for future research. Thus it cannot be termed absolutely scientific. It needs to be completed, and in fact preceded by the historical method, which consists in studying step by step the development of medical research, thought, and practice referring to the four chapters of the natural history of diseases. Only the historical method enables us to understand the particular malady and gives us scope for future research and development. In all sciences, in physics, in chemistry, in mathematics, the historical method is applied as the highest scientific method. Science without history of scientific thought is inconceivable.

Probably in no other branch of medicine is the importance of the historical method so great as in endocrinology. The study of eunuchism through this method which I now present will, I think, contribute to a better understanding of this disease. History of medicine is not an occupation for purely scholarly or dilettante minds but in its more important aspect, that dealing with the development of medical thought, is the highest scientific method in medicine. Those who cultivate it obtain a more thorough understanding of medical problems and thus a greater certitude and style in their practice.

THE ÆTIOLOGICAL CHAPTER: HOW EUNUCHISM ARISES

Eunuchism means male castration. The term arises from two Greek words meaning "bed" and "guarding" and indicates the principal function of male castrates in ancient times. The ancient Greeks used also a term meaning "cut", which in its Latinized form "spado" was used by the Romans.

Eunuchs were employed by ancient Eastern peoples such as the Assyrians, the Babylonians, the Chinese and some African peoples as special slaves or servants. Their asexuality, which, however, was not always complete, fitted them for employment as guardians and servants in harems. They were placed also in other confidential posts because, as a passage in Xenophon's *Cyropædia* indicates, being distinct from the rest

of mankind they could not be distracted by sexual considerations and adventures and would be more firmly attached to the person of their master. Such slaves were procured from prisoners of war, whom their victors castrated as a symbol of complete subjugation. This war castration was much in vogue among pre-Hellenic barbarians, as shown by ancient sculptures and paintings such as those of Karnak. Later, parents used to castrate their children so as to obtain for them a post and livelihood in the leading families. Castration for this purpose, a distinct manifestation of Eastern barbarism, was unknown among the ancient Greeks, and also among the Romans as long as they were under the influence of Greek civilization. In Imperial Rome, however, after Rome had come into contact with the Orient, eunuchs were introduced into the city, and as Gibbon writes: "The eunuchs who in the time of Augustus had been abhorrent as the monstrous retinue of the Egyptian Queen, were gradually admitted into the families of matrons and senators and of the emperors themselves." They exerted a certain rôle. Claudius heaped riches and rewards on his freedman eunuch Posides, who employed his wealth in building. Hence Juvenal's verse "*Ut spado vincebat Capitolia nostra Posides*". Such was the influence of eunuchs that in A.D. 240 the great statesman Misithenes, father-in-law of the Emperor Gordian, started his otherwise temporary reform of the Empire by expelling them from the palace. The Roman emperors took eunuchs with them into Constantinople, where they became so influential as often to dominate the Imperial court. Some of them did good work, as for example Narses, the famous general of Justinian. However, when the Byzantine court became more Hellenized the eunuchs disappeared. The slave-eunuchs of the ancient Eastern peoples disappeared later. The Turks retained such eunuchs until the fall of Abdul Hamid. In Egypt the production of eunuchs ceased with British occupation and following a convention between Great Britain and Egypt in 1877. The end of Imperial China was the end also of Chinese eunuchs. I have no precise data on Abyssinian eunuchs, although I believe that Haile Selassie succeeded in stopping that barbaric custom.

Religious eunuchs form a second class. A mystical madness led priests and followers of certain ancient Eastern religions to castrate themselves so as to devote the whole of their being to the service of their divinities. Most servitors of the cult of Cybele were castrates, and the Roman Emperor Heliogabalus is said to have subjected himself to that mutilation in order to become the chief priest of Cybele. The Jews did not of course accept castration. We read in Deuteronomy XXXIII, i: "He that is wounded in the stones or has his privy member cut off shall not enter into the congregation of the Lord." Early Christians, however, swayed by the same mystical madness as the heathens, considered that in order to devote themselves utterly to God they should remove all sexual temptations, and in some cases castrated themselves. They were seconded in that decision by a misinterpretation of certain passages in the New Testament referring to sexual sin in general. The great Origen was a castrate. Many patriarchs of Constantinople were castrates. The Valerians in the third century also castrated themselves for religious reasons. This barbaric procedure became so prevalent in the clergy that the Council of Nicea (A.D. 325) promulgated that those who had castrated themselves voluntarily were debarred from priestly offices, the interdiction not applying, however, to persons castrated for medical reasons nor to those who had been castrated against their will by barbarians.

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as castrated for medical reasons. The voices of these castrates were beautiful, and in 1877 Rossini wrote the opera "Aureliano in Palmyra" for the castrate Velutti. The custom was abolished only at the advent of Leo IX. Thus even a few years ago singer eunuchs could be encountered in Italy, as testified by Hirschfeld.

The fourth class of eunuchs comprises victims of criminal assault, of whom the most famous is the philosopher Abélard, who was attacked and castrated at the instigation of Canon Fulbert, the uncle of the seduced Héloïse. Prisoners of war forced to undergo castration belong to this category, as do the numerous castrates made by the Germans recently under the cloak of eugenics.

Finally, we have eunuchs castrated for medical or eugenic reasons. Our ancestors were somewhat lavish with this procedure. Castration was prescribed as a preventive for hernia, for certain skin diseases, and for leprosy. Ambroise Paré protested against these excesses. Nowadays medical castration is practised only on the basis of more precise indications. Eugenic castration has been abolished in favour of the less destructive ligation of the spermatic cord.

THE CLINICAL DESCRIPTIVE CHAPTER

Although eunuchs have existed since remote antiquity, a medical description of the picture presented by human castration is not found until the later nineteenth century, probably because eunuchism was not until then considered as a medical problem.

The first period of the medical study of eunuchism is dominated by the work of Goddard and of Pelikan. Even in their work the sociological and anthropological aspects overshadow clinical study. Ernest Goddard (1827-1862), a French anatomist and anthropologist, studied eunuchs during his travels in Egypt. E. W. Pelikan (1824-1884), a great authority on forensic medicine in Russia and president of the Imperial Public Health Council, studied Skoptzys. Both these authors described vaguely the macrosomia and macroskelia of eunuchs, the variations in their adiposity and their general behaviour. On the same lines Eugène Matignon, a French physician at the court of Pekin, studied the eunuchs of the Chinese Imperial Palace (1906). Some isolated studies of the skeletons of eunuchs such as that of Maiticjewski (cited by Pelikan) and of Ecker add very little. In fact all this work is only an introduction to the study of eunuchism because a precise method of exploration was lacking.

The second period, which began with the twentieth century and ended with the first world war, is one of precise anthropological research and of dawning medical study. It is dominated by Eugène Pittard, who studied principally the Skoptzys with an excellent anthropological technique made of precise mensurations and comparisons on large scales. The anthropological point of view veers more to the medical-morphological. Stimulated by this anthropological work, and principally by experimental work on animal castration, clinicians took deep interest in the whole question. Launois and Roy in 1904 and Möbius in 1906 produced the first medical studies of the morphological and psychological syndromes of eunuchs. During this period the sociological-anthropological lines of the Goddard-Pelikan era were followed by R. Millant, a young French physician killed in the first world war, and by Zambaco Pachah, a Greek physician who became personal physician to Abdul Hamid and studied the eunuchs of Constantinople. The descriptive work of Tandler and Grosz and of W. C. Koch, who studied the Skoptzys during the German occupation of Rumania, closes this period. These Austrian and German authors followed the lines of Pittard but contribute only to clarification of certain morphological details. The work of Pittard and others has demonstrated the different manifestations according to whether the castration has occurred before or after puberty. The morphological syndrome has been well studied. In pre-puberal castrates tallness with macroskelia has been emphasized. Obesity occurs principally in post-puberal castrates late after castration.

The third or contemporary period is essentially medical. Eunuchism is now regarded as an endocrine disease. This change of view and the intensity of the medical work is bound up with the triumphant development of the newest of all branches of medicine, endocrinology. We have taken from R. Martin, Ernest Pittard, Manouvrier and other anthropologists their special measurements for use, often with exaggeration, in our clinical work. However, the morphological point of view, although given undue stress by da Giovanni, Viola, Brugsch and G. Draper, is far from dominating our work. Eunuchism is studied from the point of view of its effects on all organs and systems, on psychology and behaviour, but to-day principally as regards its effects on the biochemical processes of the body, on metabolism, because metabolic disturbances are the key to therapeutic handling as they link clinical description with physiopathology.

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Later the Steinach group of Vienna completed the work of the French, American and British experimenters. Some of these experiments, such as, for instance, those on intersexualization, are very ingenious, but on the whole this group developed only details. Their interpretations went a little further than was warranted by their experimental work. A further demonstration that experimentation when not assessed in the light of clinical observation and comparative physiology (the Hunterian Tripod) is not always safe.

After the Pézard-Goodale era comes the last phase, which gives precision, to the physiopathology of eunuchism and directs treatment. It is the era of testicular hormone research. As early as June 1, 1889—a momentous date in the history of endocrinology—Brown-Séquard described at the famous meeting of the Société de Biologie in Paris the extraction of the testicular hormone through a saline solution. The idea was right, the experiment fallacious, and for many years the hormone evaded extraction. Then in 1913 Henri Iscovescu, a Rumanian working in the laboratory of Dastre at the Sorbonne, produced a more active lipid extract. Further research lagged, because chemical methods had to be perfected and a biological test evolved. This was obtained, and enabled F. C. Koch to begin his great work thirteen years later, in 1926. First with McGee and later with Gallagher, Koch—who with the modesty characteristic of great scientists put the names of his junior collaborators before his own in all his papers—produced at Chicago the first real purified testicular hormone. But extraction was difficult because tons of bull testis were required for a small yield. Nearly ten years after the first work of Koch, in 1935, Ernest Laqueur of Amsterdam and his group obtained Koch's extract from bull testis in crystalline form. Taking as their basis the work of the Göttingen chemist Adolf Butenandt, who had isolated from male urine an androgen similar up to a certain point to Koch's extract (in fact, the excretory product of Koch's extract) and determined its chemical formula, the Dutch chemists determined the chemical formula

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THE PHYSIOPATHOLOGICAL CHAPTER

Clinical medicine has undergone a complete revolution in the last forty years. Our ancestors advised leaving their theories on disease (meaning the pathogenic or physiopathological conceptions) with their overcoats on entering the clinical ward. Thus the clinician had to limit himself to a thorough examination, a good differential diagnosis, and the application of any medicine shown by purely empirical observation to be effective in the disease he had diagnosed. To-day, on the contrary, after our differential diagnosis we have to ask ourselves: "What is really happening in this patient? In what manner is his physiology disturbed?" The answer enables us to apply effective treatment, but for that we have to bring our physiopathological knowledge to the bedside. This knowledge is of course more precise than the pathogenic speculations of our ancestors. It is based on experimentation and has been controlled by clinical results. Even so, physiopathological reasoning is difficult and may be dangerous. It is necessary, however, unless we wish to remain in the therapeutic nihilism of the nineteenth century. To be a good clinician in the modern sense of the term does not mean merely to have qualities of observation adequate for a good differential diagnosis, but means also to have physiopathological, mainly biochemical, knowledge and the power of accurate reasoning so as to determine what is wrong in the physiology of the individual patient.

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President—Sir WALTER LANGDON-BROWN, M.D.

[May 22, 1946]

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INAUGURAL ADDRESS

By Sir WALTER LANGDON-BROWN, M.D.

IN the first place I must congratulate those who have worked so hard for the public recognition of the status of Endocrinology on the success of their efforts, of which the institution of this Section is an outward and visible sign. Next, I would express my deep appreciation of the honour you have done me in electing me your first President. Of recent years I have merely been an interested spectator on the bank of a swiftly flowing and expanding stream of research. Indeed, the only justification for my accepting the distinction you have conferred upon me is that from the onset I have been actively interested in the development of endocrinology. It will, therefore, be fitting that I should devote the greater part of my Address to the history of those early years.

I

Modern endocrinology dates from 1891. A Committee had been appointed to investigate the cause of myxœdema, which was recognized to be associated with the failure of function of the thyroid gland. But the tendency was to regard the disease as due to a failure of excretion, which, indeed, the bloated aspect of the myxœdematous patient might well suggest. Halliburton regarded the accumulation of mucin in the tissues as evidence of this, but it was soon shown that there was a similar infiltration of all the subcutaneous tissues. Victor Horsley was the secretary of this Committee and G. R. Murray, who had worked with him at University College Hospital, suggested that the condition was due not to a failure of excretion but to the loss of an active internal secretion. To emphasize his faith in his hypothesis, he showed a case of myxœdema at a meeting of the Newcastle and Northumberland Medical Society, and said that he proposed to treat it by an extract of thyroid gland. I had the story of what followed from Murray's own lips. A senior member of the Society said that it would be just as sensible to treat a case of locomotor ataxy with an emulsion of spinal cord! Undeterred, Murray made arrangements with a slaughterhouse to be allowed to dissect out sheep's thyroids under antiseptic precautions. The Medical School at Newcastle refused him any facilities, but Armstrong College came to his assistance and gave him a room in which to prepare his extracts. A year later he triumphantly showed the case of myxœdema which had been cured by his extracts before the same Society. When Hector Mackenzie in the following year showed that the extract could be taken in a tablet form, by the mouth, thyroid therapy leapt ahead. Indeed, its early triumphs proved later to be disappointing because it was too hastily assumed that other gland extracts were potent by the same route.

of Koch's extract and named it testosterone. A few months later the Yugoslav chemist Ruzicka, working in Zurich, obtained the hormone synthetically from cholesterol.

The cycle has closed. The visionary "semen" of Aretaios, the speculative "particles imbued with seminal tincture" of Thomas Willis, the X substance of John Hunter and of Berthold, have been thrown into the crucible of the biochemist, who has obtained its intimate construction and is thus able to reproduce this "vital" force from inert substance. . . . The philosopher's stone of the old alchemists has not been an empty dream.

Science, however, never stands still. Work now in progress is leading to discovery of a second testicular hormone, inhibin. Further, we are no longer arrested at the simple formula eunuchism—lack of testicular secretion. Steinach and his group were romancing on the erotization of the cerebral cortex by the sexual hormones, and explained everything in eunuchism, including the mental outlook, by lack of testicular hormones. Their fantasies dragged endocrinology into a period of "glands of destiny," of "glands regulating personality." Glands explained everything, from the conjugal quarrels of a suburban household to the military genius of a Napoleon and the sadistic barbarism of a Hitler. Contemporary work has shown that the endocrine glands and thus the testis are parts to a great system of metabolic or constitutional regulation and correlation. In eunuchism it is not the deficiency of the testis which explains everything, but the reaction of the other elements of this system of constitutional regulation, of the other endocrines, of the nervous vegetative system, of the psyche. The individual variations in eunuchism are explained by the differences of compensation of the other elements of the system of constitutional regulation. For this reason there are eunuchs whom the loss of the testis transforms into pessimistic melancholic individuals, and others who like Narses are capable of resounding military feats. For this reason there are eunuchs incapable of any sexual intercourse and others who maintain their potency.

Thus step by step, from a vague conception of connexion between "semen" and virility, through the conception of lack of testicular internal secretion, we have reached the conception of total disturbance of the system of constitutional regulation, starting with deficiency of the testis but depending on the individual capacity of this system of constitutional regulation.

THE THERAPEUTIC CHAPTER

The therapeutic chapter has developed in parallel. In times when there was no adequate physiopathology of male eunuchism treatment was lacking or was purely empirical. Methods were applied which had been demonstrated by clinical observation to be effective in similar diseases. Far be it from me to belittle the importance of the clinical empirical method in therapy. It is a great method and in the last resort the one at which we shall always end. We cannot limit ourselves to clinical empiricism, however, it cannot be our beginning and our end. True modern therapy consists in the application of therapeutic methods on the basis of physiopathological thinking, but with absolute control of this application by the clinical empirical method.

When physiopathology centred on the lack of testicular hormone, the treatment of eunuchism became endocrinotherapeutic. Hormones were applied, their clinical application, indications, dosage and other details being strictly controlled by the clinical empirical method. The perfecting of hormonal preparations, the introduction of the method of pellet implantation, and the finding of effective oral preparations mark successive steps in progress.

Nowadays, when physiopathology has centred on consideration of total constitutional reactions (real total psychosomatic personality reactions) treatment has become constitutional. Endocrinotherapy remains as a basic procedure, but other general constitutional procedures such as physical methods and psychotherapy are added.

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It will be agreed, however, that we have now passed far beyond the birth of modern endocrinology. But one cannot omit reference to the fruitful co-operation of the surgeon, in the treatment of hyperthyroidism, hyperparathyroidism, the adrenogenital syndrome and, more recently, the treatment of myasthenia gravis by thymectomy. However, it will be of interest to review the general biology of the endocrine system in the broadest terms.

II

The enormous energy developed in the zygote provides the impetus which carries the organism on its passage through life. It is perhaps somewhat fanciful but it does remind one of the release of atomic energy. At that moment growth is at its maximum and measured in fractions from that original impetus there is a steady decline in the rate of growth. It has even been asserted that at the moment of birth not more than 2% of that original impetus remains. The organism may be compared to a projectile whose initial velocity constantly diminishes from the moment of its discharge. It does not escape from the second law of thermodynamics, though, as Hopkins shrewdly pointed out, it is the function of life to hold up that dissipating energy at a useful level.

For the last twenty years and more interest has concentrated, however, on the quality rather than on the quantity of growth. The experimental embryological studies, particularly of Roux and of Spemann, revealed amazing facts about the "organizer". At an early stage the graft of embryonic tissue from the dorsal lip of the blastopore is capable of imposing its inherent potentialities on its new environment. As we know, in this way a neural canal is formed on any part of the embryo receiving the implant. Yet at a slightly later stage the implant has to accept the structural development of its host. Clearly specialization of organizing material has already begun. A new interest was aroused by Joseph Needham's demonstration that this "organizer" did not depend on cellular structure; the potent material could be crushed, frozen, or even boiled. Indeed, boiling seemed to set it free and increased the scope of its activities. Therefore it obviously was not a ferment. He found that chemically it was a sterol, reminding us at once of the chemical structure of certain hormones. All this work proves that chemical controls are actively at work before any trace of a nervous system has appeared.

Indeed, it is freely recognized that organisms are controlled by several mechanisms before any semblance of a nervous system has appeared in evolution. Chemotropism may be the most powerful but by no means the only control of this order. It lies too far outside my present topic to give illustrations of stereotropism, heliotropism and so forth; though the subject opens a fascinating vista. We are concerned at this stage with the chemical controls and may regard hormones as a specialized and concentrated form of this. In other words, hormones appeared before the glands which were to house them. Comparative morphology presents a good deal of evidence that many of the recognized endocrine glands had a more primitive function than that which they now possess. Thus in the worms and *Peripatus* there are paired nephridia in every segment. By their means the function to which Claude Bernard attached such fundamental importance, the constancy of the internal medium, is secured. In higher forms of life changes in structure and habitat rendered this method unsuitable. The posterior nephridia were condensed to form the functioning metanephros while some of the more anterior ones became modified to house some of the endocrines. In fact the whole process reminds us of the hermit crab which existed before it found an empty whelk shell for an abode. Thus J. F. Gaskell, continuing his father's researches, showed that in the lamprey there was a wide distribution of adrenalin-secreting cells, though as development increased these became almost entirely confined to the medulla of the adrenal.

Considering the struggle the central nervous system displayed to obtain control of the body it is not likely that it would abdicate in favour of mere chemical controls. The anatomical arrangements of the sympathetic nervous system admirably adapts it to the rapid production of widespread effects. Failure to recognize this was the error into which earlier endocrinologists fell; although the close anatomical association between the nervous and glandular elements of for example the pituitary and adrenal should have prevented this. This close association having once been achieved it was never dropped, showing that it must be of great advantage to the organism. Pathology illustrates this by the observation that in anencephalic monsters the fusion between cortical and medullary portions of the adrenal does not occur.

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The next phase was the discovery of an active adrenal extract. A good deal of work was being done on tissue extracts in general, which were all found to *lower* blood-pressure. Oliver, a physician practising in Harrogate, declared to Schaefer that he had prepared an extract from the adrenals which *raised* blood-pressure. Somewhat sceptical, Schaefer, nevertheless, invited Oliver to come to University College, London, to work at the subject, and was convinced. Naturally this roused fresh interest in Addison's disease, but strangely enough a failure of excretion on the part of the adrenals, anatomically so close to the kidneys, to detoxicate the body was regarded as the explanation, until Humphry Rolleston in his Goulstonian Lectures for 1895 adduced evidence of its being an "atony" due to the loss of some internal secretion. The isolation of adrenalin soon followed, but as comparative studies showed that adrenalin was purely the production of the medullary portion of the gland we were completely misled as to the real cause of Addison's disease until the work of Stewart and Rogoff. In the same way the real importance of Langley's generalization that the effect of adrenalin on any part was the same as stimulation of the sympathetic nerves to that part was not fully grasped, indeed not until Dale's demonstration of the wide distribution of adrenergic fibres.

Meanwhile Schaefer and Oliver's discovery of an active pituitary extract gave the final blow to the excretory theory of endocrine glands, bringing down with it many then fashionable theories of auto-intoxication. Yet so attractive is the idea to many minds that more than twenty years later it was suggested that hyperparathyroidism was due to a failure to eliminate guanidine.

Bayliss and Starling's discovery of secretin in 1902 was full of theoretical interest but has proved disappointing therapeutically. Taken in conjunction with Pavlov's work on "sham feeding" and "appetite juice" it rather upset the balance of our views as to the relative importance of chemical and nervous factors. Starling was inclined to regard the initial step in digestion as nervous in origin, starting a succession of chemical reactions, the forerunner in each case being necessary to stimulate the next in series. Considering the way in which the nervous system developed increasing control throughout evolution this seemed improbable. Another pointer which was missed for some years was the double nervous and glandular structure of the pituitary and adrenals.

This was the state of affairs when Starling brought forward his hormone theory in his Croonian Lectures for 1905. The name was suggested by W. B. Hardy—meaning a stimulant of chemical origin to act on other structures at a distance. The foundation of a scheme of this sort led to a great increase of interest and research in the whole field of endocrinology. Before long, however, the idea of independent autonomous glands without any central control was modified and that of the integration of the endocrine system began to replace it. This was largely due to increasing recognition of the leading importance of the pituitary gland with its obvious interactions with the other glands. I ventured to call the pituitary gland "the leader of the endocrine orchestra", though later when the importance of the hypothalamus in relation to the pituitary became clearer it seemed more accurate to regard the hypothalamus as holding the still more important rank of conductor of that orchestra.

The search for separate hormones in the pituitary was too amply rewarded, for at least eleven were described! This seemed improbable as the gland only contains three types of cells and there seemed little point in a separate lactogenic hormone which might never be called upon to act throughout the life of the female and never in that of the male. And so the conception arose of the secretions of the cells being modified through the hypothalamus in accordance with the needs of the body. We can, therefore, conceive of a steady autonomous action of the endocrines controlled through the hypothalamus and pituitary as needed.

Meanwhile the clinician was receiving most important aid from the organic chemist. This introduced a much more scientific attitude to the whole subject. One has only to compare Starling's Croonian Lectures with Dodds' Goulstonian Lectures for 1934 to realize the significance of the advance. Here we were shown the importance of a basal group which could be modified to form different hormones and the close relationship between such substances and the stimulators of irregular growth, i.e. the carcinogenetic substances. Perhaps a particularly surprising feature of the work was the demonstration that a synthetically prepared substance of simpler chemical constitution than that prepared by the body could "pick the physiological lock". It may be asked, why should the body go to the trouble of preparing the more elaborate substance? Really the answer is simple. The natural product is formed under strict limitations of temperature, pH and many other physical conditions, whereas the laboratory procedures would be fatal to the cell. The synthetic production of hormones became recognized as possible and very important.

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recognition of cholinergic and adrenergic nerve endings that every nervous stimulus was mediated through a chemical mechanism before affecting the tissue cell. This generalization has greatly clarified our whole outlook.

Although the essential cause of cancer is still unknown it would be generally agreed that it is characterized by a complete breakaway of the growth factors from nervous control. It is, therefore, not surprising that the chemical similarity between hormones as regulators of normal metabolism and carcinogens as stimulators of abnormal growth has excited much interest and perhaps not unnaturally some apprehension. This association between all growth-promoting and differentiation-promoting agents comes out in a very striking way if amphibian eggs are subjected to what is known as "delayed fertilization". To quote Joseph Needham's account of the work "the longer the eggs wait for the sperm cells the more virulent is the subsequent dislocation of development. If the delay is short, serious unbalance of the sex-ratio ensues (due to interference with the formation of the sex hormones?); if the delay is longer, multiple liberation or formation of the organizer takes place, and multiple monsters result; if the delay is very long, development runs an extremely abnormal course, giving shapeless teratomata and these if implanted into an adult frog will give malignant growth, including even metastases. This gradual transition from the normal to the frankly malignant must surely depend on purely environmental factors. It is, indeed, in connexion with the sex hormones that the overlap between the stimulus for cancer production and the stimuli for the sexual cycle is most obvious. But this overlap is also seen between the oestrogens and the primary organizer. Thus Waddington and D. M. Needham were able to produce secondary neural axes in host embryos by the implantation of certain synthetic oestrogenic hydrocarbons. There is strong support for the opinion that the primary organizer is a sterol-like substance. In view of the exceedingly wide distribution of the primary organizer and the presence of oestrogens in coal-tar, it is significant that oestrogens have been found to exist in some plant tissues. This at once reminds us of those other exogenous hormones, the vitamins, but I am deliberately excluding them from this survey, other than to refer to the sterol-like character of vitamin D; thus providing us with another example of overlap between the various growth factors.

The part played by hormones both in physical and psychological manifestations is so closely interwoven in the whole organism that while taking a special interest in them we incorporate them in the general body of medicine. This would accord with the present tendency to adopt a psychosomatic attitude in medicine.

Clinical Section

President—A. DICKSON WRIGHT, M.S., F.R.C.S.

[March 8, 1946]

Addison's Disease and Pregnancy.—S. LEONARD SIMPSON, M.D.

This is a case of Addison's disease in a woman of 30, characterized by the onset of symptoms during pregnancy some four years ago, and the occurrence of a second successful pregnancy, terminating in a second live child recently, but with failure of lactation after both parturitions. I have seen two other patients with Addison's disease survive pregnancy and a few have been published, but this patient appears to be the first recorded example of Addison's disease and two pregnancies, as well as two live children. Pigmentation occurs physiologically during pregnancy in normal women, probably due to temporary inadequacy of adrenal function, the physiological hypertrophy of the adrenal cortex indicating that the increased function is called for by pregnancy, the undestroyed portion of the adrenal gland in Addison's disease being sufficient in the earlier phase of the disease for normal purposes but not for the added requirements of pregnancy.

The patient married some five years ago, and became pregnant after six months. Some pigmentation of the face and hands was noticed during the fifth month of this first pregnancy, and from that time the patient complained of tiredness and malaise. However, the pregnancy and parturition were normal but lactation failed. The first child was born in December 1943. Although lactation failed, amenorrhœa persisted until August 1944, when normal monthly menstruation occurred and continued, but an occasional period was missed. Her health was indifferent, and general malaise was noticed. The pigmentation, which had faded somewhat after parturition, gradually returned, and she lost two stone in weight. In August 1944, the patient was admitted to Queen Elizabeth Hospital, Birmingham, in semi-coma, and with a blood-pressure of 80/60. The diagnosis of Addison's disease was made, and she responded to intravenous saline and later maintained imperfect health on 4 grammes of salt a day without cortical extract.

The patient was first seen by me in November 1944, complaining of weakness and malaise. She had pigmentation of the skin, as in Addison's disease, but not of the mucous membranes. She was still taking salt. Her blood-pressure was 90/60; serum potassium 20.1 mg., serum sodium 305 mg. and serum chloride 586 mg., and the Kepler test was positive for Addison's disease, under 12.4. She responded clinically to 10 c.c. eucortone daily, and after some weeks, to 5 mg. of desoxycortone daily instead of the eucortone; and the sodium chloride was increased to 8 grammes a day. Her blood chemistry became normal on this dosage. In February 1945, I implanted in the subcutaneous tissue of the abdomen 6 by 100 mg. of desoxycortone, and continued the salt intake of 8 grammes a day. The patient remained very well. B.P. 120/80. In May 1945, she complained of two months' amenorrhœa. This was at first thought to be part of

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was almost identical with that of his brother. The right testis was infantile but in the scrotum. The left was ectopic and palpable just over the pubis. His height was 67 inches. (fig. 2.) He responded in similar fashion to a testosterone implant.

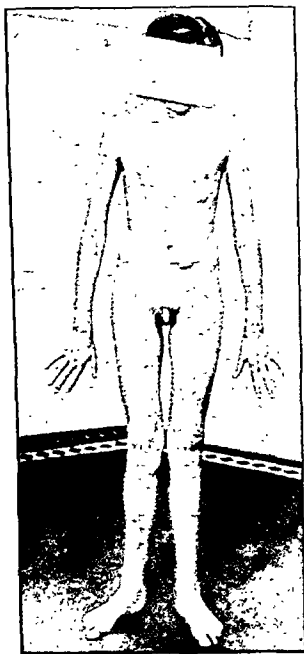


FIG. 1.
Thomas, aged 18.

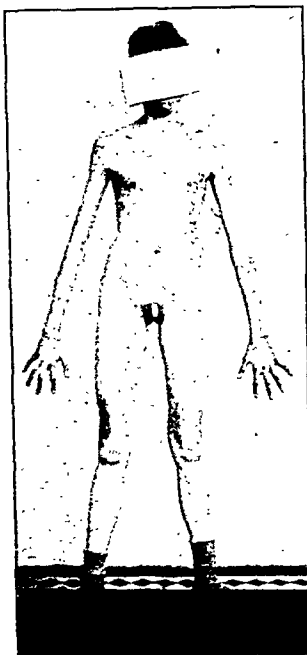


FIG. 2.
Daniel, aged 22.

Differential diagnosis.—Infantilism involves (1) infantile sexual development; (2) sub-normal growth in height and breadth; (3) delay in epiphyseal union, and (4) a graceful delicate appearance (Levi-Lorain type). The primary defect in infantilism is pituitary, the gonadal defect being secondary.

In eunuchoidism there is a primary failure of gonadal development. The height is usually above normal, but may be normal, and the span is greater than the height. It is rarely recorded as below average normal, although I have such definite cases. Eunuchoids are usually described as being adipose, but it is not generally recognized that both eunuchoids and pre-pubertal castrates may be quite thin. (I have one example of the latter.) Growth continues until the late twenties, or later, as the epiphyses are ununited and the pituitary growth hormone continues to be secreted. Both patients had mumps at the age of 5, but as far as is known, this was not complicated by obvious orchitis.

In view of the continued growth in height and the failure of response to gonadotrophic hormone, as well as the eunuchoid proportion of span and height, I favour the diagnosis of eunuchoidism in these brothers. (The estimation of gonadotrophins in blood and urine was not carried out.) It is probable that their ultimate height may be well above normal. However, both of them, at the age of 14 or even 16, were well below the average height of their friends. They were below 5 ft. in height. It is not generally recognized that this may be the case in eunuchoids, and was true in one of my eunuchoid patients who is now 6 ft. 3 in. The cause of this is probably the absence of testosterone secretion, which providing that it does not produce closure of the epiphyses, has an important stimulating effect on growth. It would therefore appear that at the age of 14, or even 16, these two brothers gave a clinical picture of infantilism, although to-day the correct diagnosis appears to be eunuchoidism.

Gynæcomastia with Bilateral Undescended Testes in a Man aged 21.—J. S. RICHARDSON, M.D. (St. Thomas's Hospital).

Raymond D., aged 21, first noticed swelling of his breasts at the age of 16, at which time they were tender and painful. They have remained enlarged but have been less tender during the last year. He experiences more pain when the weather is cold. The

the adrenal disorder, as she had missed menstruation occasionally. In August 1945, on abdominal examination, a swelling was felt in the suprapubic area, and pregnancy was discovered. She remained very well, although the blood-pressure was 98/60, and serum sodium 307 mg. The serum chloride was 618 mg. and potassium 17 mg. There had been no disturbance of any kind during the initial period of pregnancy. She continued very well throughout the pregnancy on 5 mg. desoxycortone injected daily, and 12 grammes of salt daily, the blood-pressure averaging 100/75.

As Willesden General Hospital has no obstetric department, she was transferred for the parturition to Central Middlesex Hospital under Dr. Avery Jones and Mr. J. S. McVine. Treatment was continued with desoxycortone, with salt, as previously, and without any change. On November 30, 1945, she was delivered of a male baby, weight 6 lb. 10 oz., after a normal labour of sixteen hours. The baby was normal except for a mild degree of hypospadias. Her systolic blood-pressure remained between 100 and 120 mm.Hg, and there were no unusual symptoms. Lactation, however, failed, and artificial feeding difficulties were met with but overcome.

The patient was seen by me on January 4, 1946, and was very well. On January 18 she complained of swelling of the face. Blood-pressure was 160/105. This indicated excessive treatment. The desoxycortone was continued, but salt therapy stopped. On February 1 she was very well, B.P. 140/100. A clinical assistant saw her and again ordered 8 grammes of salt a day. The œdema of the face returned; and salt was then again stopped.

The patient is now in good condition. B.P. 125/80.

Comment.—Pregnant animals survive adrenalectomy for longer periods than normal animals. This may be due to hypertrophy of the anterior pituitary gland with (a) increased secretion of diabetogenic hormone, (b) increased secretion of adrenocorticotrophic hormone which stimulates accessory adrenal cortex tissue and (c) increased secretion of progesterone. In women, the uninjured part of the adrenal cortex probably undergoes hypertrophy and there is also a possibility of the adrenal cortex of the fœtus helping to compensate for the mother's deficiency. It is known that the adrenal cortex plays an important part in lactation, which fails in adrenalectomized animals maintained on inadequate doses of cortical extract. The patient might have lactated if the desoxycortone had been replaced by cortical extract containing the carbohydrate corticosterone factor.

Two Brothers, with Infantilism or Eunuchoidism.—S. LEONARD SIMPSON, M.D.

These patients are presented because of the rarity of the condition, and the differential diagnosis.

Thomas, aged 18, was first seen by me at Willesden General Hospital Endocrine Clinic in September 1945, being referred for "undeveloped testes". He had a boyish appearance, and shy, diffident manner. His weight was 7 stone, height 67 inches, and span 71 inches. His shoulders were slightly broader than his pelvis, but his general appearance was graceful and fragile. His fingers and toes were long and slender. There was an absence of fat generally. The penis was tiny and the testes not palpable. No hair was present on the face, pubis or axillæ, and the voice was high-pitched and unbroken (fig. 1). B.P. 125/80. Pulse 80. Fundi normal. X-ray (Dr. Rohan Williams): "Pituitary fossa smaller than average; delayed epiphyseal closure—average for male of 15". 17-ketosteroids in urine (Dr. W. Payne): 4.6 mg. per day; 3.2 mg. per litre.

Treatment.—In October 1945, I implanted under local anaesthesia 8 tablets of 100 mg. each of testosterone propionate in the subcutaneous tissue of the abdomen.

Result.—Frequent penile erections started after one week. Appetite, weight (1 stone in four weeks) and strength were greatly increased. He had increased 1 inch in height, and his shoulders were broader. The voice was deeper. The penis was enlarged, and there was an interesting area of redness (erythema) over the pubis, pelvis, and scrotum. Some hair was growing on the pubis. To-day his weight is 9 stone 3 lb. and his height 69 inches. Hair is plentiful on the pubis (but limited horizontally) and in the axillæ but little on the face. His manner is much more forthcoming and enterprising. The penis is larger; the right testis is infantile and now felt in the scrotum; the left is not palpable.

The brother, Daniel, aged 22, came to hospital because of the great improvement in Thomas, and because he had failed to respond in any way to a course of chorionic gonadotrophins (500 units injected twice weekly for six weeks). His general appearance

was almost identical with that of his brother. The right testis was infantile but in the scrotum. The left was ectopic and palpable just over the pubis. His height was 67 inches. (fig. 2.) He responded in similar fashion to a testosterone implant.

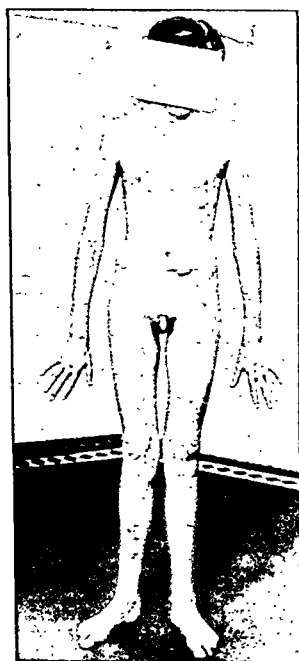


FIG. 1.
Thomas, aged 18.

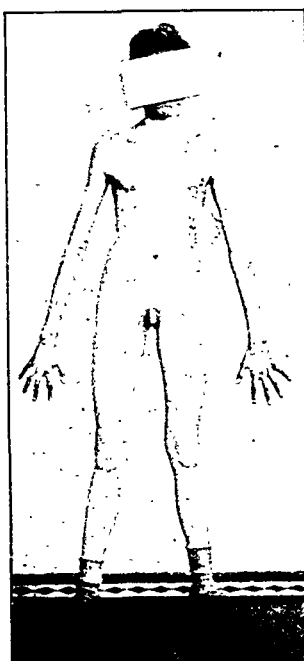


FIG. 2.
Daniel, aged 22.

Differential diagnosis.—Infantilism involves (1) infantile sexual development; (2) sub-normal growth in height and breadth; (3) delay in epiphyseal union, and (4) a graceful delicate appearance (Levi-Lorain type). The primary defect in infantilism is pituitary, the gonadal defect being secondary.

In eunuchoidism there is a primary failure of gonadal development. The height is usually above normal, but may be normal, and the span is greater than the height. It is rarely recorded as below average normal, although I have such definite cases. Eunuchoids are usually described as being adipose, but it is not generally recognized that both eunuchoids and pre-pubertal castrates may be quite thin. (I have one example of the latter.) Growth continues until the late twenties, or later, as the epiphyses are ununited and the pituitary growth hormone continues to be secreted. Both patients had mumps at the age of 5, but as far as is known, this was not complicated by obvious orchitis.

In view of the continued growth in height and the failure of response to gonadotrophic hormone, as well as the eunuchoid proportion of span and height, I favour the diagnosis of eunuchoidism in these brothers. (The estimation of gonadotrophins in blood and urine was not carried out.) It is probable that their ultimate height may be well above normal. However, both of them, at the age of 14 or even 16, were well below the average height of their friends. They were below 5 ft. in height. It is not generally recognized that this may be the case in eunuchoids, and was true in one of my eunuchoid patients who is now 6 ft. 3 in. The cause of this is probably the absence of testosterone secretion, which providing that it does not produce closure of the epiphyses, has an important stimulating effect on growth. It would therefore appear that at the age of 14, or even 16, these two brothers gave a clinical picture of infantilism, although to-day the correct diagnosis appears to be eunuchoidism.

Gynæcomastia with Bilateral Undescended Testes in a Man aged 21.—J. S. RICHARDSON, M.D. (St. Thomas's Hospital).

Raymond D., aged 21, first noticed swelling of his breasts at the age of 16, at which time they were tender and painful. They have remained enlarged but have been less tender during the last year. He experiences more pain when the weather is cold. The

breasts have never secreted. His voice has not broken but pubic hair appeared at the age of 14 and his penis began to enlarge at that time continuing to do so until he was 20. His sexual interests are homosexual and he suffers from prolonged and frequent erections but has never had ejaculations.

Previous health.—Mumps, measles, chickenpox before the age of 10. An operation for bilateral hernia at the age of 7; no information as to whether left testis was removed is available.

Family history.—No evidence of endocrine disorder. Patient is youngest of five by fifteen years.

On examination.—He is a poor physical specimen without a beard and with scanty body hair. Height 68½ in.; span 68½ in.; sole to pubis 34 in. He has bilateral gynæcomastia with easily felt glandular tissue and the aureolæ are pigmented without being enlarged. His penis is large; his left testis impalpable; the right at the external inguinal ring is small; the prostate is very small. Urinary hormone assays—17-ketosteroids, 16.4 mg. in twenty-four hours; alpha fraction 80-90%; follicular stimulating hormone (F.S.H.) 320 M.U. in twenty-four hours; no luteinising effect; œstrogens in urine—10 gamma in twenty-four hours.

It is thought that this case is an example of the syndrome described by Klinefelter *et al.* (1942) and expanded by Nelson and Heller (1945). Our case had bilateral gynæcomastia occurring in an adolescent with presumptive evidence of tubular degeneration, as there was bilateral cryptorchidism. The Leydig cell function was adequate as evidenced by a large phallus and normal quantitative and qualitative 17-ketosteroid excretion and there was excess follicular stimulating hormone (F.S.H.) in the urine. It is known that eunuchoids and castrates who have excess F.S.H. and only extratesticular androgen do not get gynæcomastia but that these, if adolescent, may develop gynæcomastia when treated with testosterone.

It is tentatively suggested that the development of gynæcomastia in the group of cases to which we believe this one belongs, depends on an excess of F.S.H. and the presence of an adequate supply of androgen.

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Chronic Idiopathic Hypoparathyroidism.—J. S. RICHARDSON, M.D. for H. GARDINER-HILL, M.D., F.R.C.P.

N. C., aged 16, was first admitted to St. Thomas's Hospital under the care of Dr. Gardiner-Hill on April 25, 1941. He was 7 lb. at birth and walked late—at 2 years. He first had epileptiform fits at 18 months and these continued intermittently until he was given epanutin at the age of 10. Various diagnoses were made such as epilepsy, poliomyelitis and spastic diplegia, the last two because of the deformity of his legs and feet. These were first noticed when he began to have severe cramps in his legs and later arms, at the age of 5. His feet turned in and he had difficulty in walking, with almost constant spasm that had been worse for two years.

On examination he had a strongly positive Chvostek's sign and carpopedal spasm with bilateral pes cavus. The blood calcium was 4.1 mg.%; inorganic phosphate 9.9 mg.%; blood urea 37 mg.%. Urine normal. Bilateral cataract. No significant changes in his bones.

Treatment.—Parathormone 60 units daily for fourteen days did not control his cramps and he had several epileptiform convulsions. Blood calcium 5.4 mg., phosphate 8.8 mg. Treatment was changed to ostelin 120,000 units and calcium gluconate one ounce daily. After three weeks, the calcium was 8.2 mg., phosphate 7 mg. and after five weeks calcium 8.2 mg. and phosphate 4 mg. These figures remained more or less constant for several months. He was discharged on January 1, 1942 on 150,000 units of ostelin and one and a half ounces of calcium gluconate daily, the blood calcium then being 10.2 mg., phosphate 6 mg. All other investigations proved negative except the blood urea that remained round about 40 mg.

After an operation for bilateral pes cavus in June 1943 his blood calcium was 18 mg.%. No evidence of metastatic renal calcification was found. From that time he has been on halibut liver oil capsules 1,000 units and calcium gluconate half an ounce daily, with a calcium level of about 9.0-11.0 mg. and inorganic phosphate of 4 mg. On February 20, 1946, his serum calcium was 8.0 mg., inorganic phosphate 4.4 mg.

These cases of chronic idiopathic hypoparathyroidism are rare. Rose in 1943, could only find some 70 odd in literature. The association of epilepsy is well recognized but only recently have E.E.G. changes, suggestive of epilepsy, been demonstrated in hypoparathyroidism, and these made to disappear by adequate medical treatment or surgical implants (Odoriz, 1944, Taubenhau and Engle, 1945). This case did not respond to parathormone but was well controlled by large doses of vitamin D, and in this is similar to three cases described by Albright *et al.* (1942).

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Hypogonadism (Eunuchoidism) with Ununited Epiphyses.—HUGH DUNLOP, F.R.C.P. and PHILIP ELLMAN, F.R.C.P.

G. T. F., aged 36, cook, was referred to the Out-patients Department of one of us (P. E.) at the Rheumatism Unit at St. Stephen's Hospital as a case of "rheumatism."

He complained of pain in the left shoulder and forearm on and off since 1938. He has had similar pain in right shoulder and lumbar region.

Previous history.—1924, influenza.

On examination.—Pallid individual, "myxoedematoid" facies, looking younger than his age with a rather effeminate voice; hair on face and axillæ very scanty, no hair on the chest and pubic hair is of feminine type with a concave upward margin. He shaves only once every three weeks. External genitalia normal; testes descended and normal.

Heart, lungs, abdomen, central nervous system, were normal. Blood-pressure normal. Pulse 58.

Examination of the locomotor system shows large hands and feet with long slender fingers (figs. 1 and 2).

No pain, tenderness or swelling of the joints. He has limitation of extension of the elbows due to a chondroostrophy.

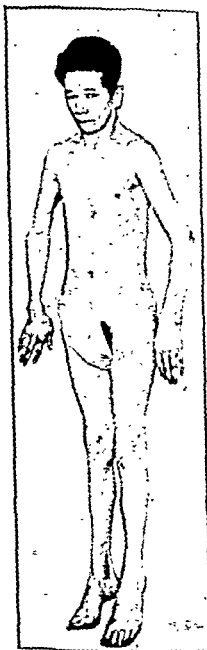


FIG. 1.

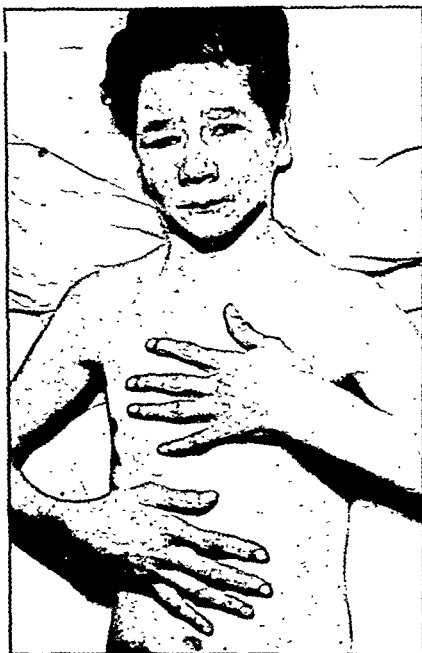


FIG. 2.

Note the myxoedematoid facies, absence of hair on the chest, large hands and long slender fingers.

X-rays of his hands, knees, and feet show delayed union of the epiphyses with an epiphyseal age of about 18.

X-ray of skull shows a deep pituitary fossa, which is normal in size.

All urinary investigations were normal. Volume of urine 1,360 c.c. per day. 17-ketosteroids 3.3 mg. per litre or 4.5 mg. per day.

Blood-count normal. Blood cholesterol 141 mg. %.

He was referred by one of us (H. D.) to Mr. Broster's Endocrine Clinic where he was considered a suitable case for testosterone implant of 600 mg. which up to date he has refused.

The delay in union of the epiphyses is consistent with the diagnosis of hypogonadism.

Whether this is a so-called "primary" hypogonadism, or due to a defect elsewhere in the endocrine system, is debatable.

Cushing's Pituitary Basophilism treated successfully by Deep X-ray Therapy.—PHILIP ELLMAN, F.R.C.P., and G. VILVANDRÉ, M.R.C.S., L.R.C.P.

Case shown to the Clinical Section by one of us (P. E.), November 1934 (*Proc. R. Soc. Med.* 28, 335). She had several courses of X-ray therapy until 1939 and we have convincing evidence of its beneficial effects in this case.

Her general appearance is now normal; she has lost her hirsutism and her florid complexion. She is now no longer obese; she has lost an appreciable amount of weight—weight loss from 9 st. 3 lb. to 8 st. Her blood-pressure is normal, 120/70. There are no abnormal findings in the cardiovascular system. Central nervous system normal.

She has no pigmentation of the legs or discoloration of the skin.

All urinary investigations are negative.

Her blood-count is normal; there is now no œdema.

X-ray treatment has proved beneficial in so far as: (1) There has been a resumption of menses with normal loss. (2) Blood-pressure is normal. (3) There is now no polycythæmia. (4) Her appearance is normal and her weight is now normal. (5) Her condition has shown progressive improvement to practically a normal state since it was first detected in 1934. (6) She has no headaches.

Mr. Northfield has seen her and has regarded the results as so satisfactory that any question of surgery does not arise.

Dr. A. C. CROOKE: It is difficult to assess the effect of any treatment in Cushing's disease because of the natural fluctuation in severity of the symptoms from time to time and because occasionally symptoms disappear completely without any treatment. Cushing originally claimed that radiotherapy was the treatment of choice but I have sections of the pituitary glands of his patients which he once claimed to have cured! Our own experience of radiotherapy has been equally disappointing and I have had the opportunity of examining sections of pituitary glands from patients who have died in spite of intensive X-ray treatment and found no histological changes in them. This is in marked contrast to the large areas of necrosis caused by the implantation of radon seeds into the pituitary gland which results in a dramatic cure of basophilism in a short time. The purple striæ atrophicæ change to pink within twenty-four hours, the patient loses weight and the other symptoms subside more gradually. This method of treatment was first described by the late Mr. Pattison in 1938 and seems to me to be the most promising one at present available but it is liable to cause signs of pituitary insufficiency if too large a dose is given.

REFERENCE

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Male Gynæcomastia: Testicular Atrophy.—A. C. CROOKE, M.D.

K. E., a married soldier, aged 24, complains of painful swelling of the right breast of eight months duration. Subsequently the left breast became similarly swollen and painful. An operation was performed at the age of 14 to bring the right testicle down into the scrotum but it subsequently retracted. The left is in the normal position but has always been rather small. He has normal intercourse but no ejaculations. Pubic and axillary hair appeared at puberty but he only shaves twice a week and his voice has never broken.

On examination.—Masculine habitus except for a diffuse tender enlargement of the right breast and less of the left. Large areolæ and nipples. Scanty moustache and beard and female distribution of pubic hair. Penis and scrotum normal but testes small.

17-ketosteroid output 23 to 25.9 mg. in twenty-four hours.

Testicular biopsy: Marked atrophy of seminiferous tubules and great hyperplasia of interstitial cells.

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Section of Medicine

President—T. IZOD BENNETT, M.D., F.R.C.P.

[April 30, 1946]

Treatment of Ulcerative Colitis with Intestinal Mucosa

By A. MORTON GILL, M.D.

Study of the natural course of ulcerative colitis, with its tendency to spontaneous remissions and relapses, led me to consider whether, in some cases at least, the condition might not be the result of a deficiency. Preliminary investigations suggested that this deficiency might result from lack of some factor and that this hypothetical factor might be produced in or by some portion of the small intestine. This idea could best be tested by feeding raw small intestine to a victim of ulcerative colitis who had failed to respond to orthodox therapy and who had gone for a long time without remission of his disease.

About nine years ago there came under my care a man who had had the disease for three years, including one year in hospital, without showing improvement. Treatment with raw pig's small intestine by mouth resulted in a remission which was maintained so long as he took the treatment. When supplies failed (fig. 1) he relapsed. When supplies were again obtainable he became well. Figs. 2 and 3 show what happened when he voluntarily ceased treatment and when he started it again, namely, first a relapse and then a remission. At this time dried preparations of pig's small intestinal mucosa became available. There were two preparations, A (Benger's) in which enzymal activity was retained and B (Allen and Hanbury's). On A there was little or no improvement, on B a complete remission within a month (fig. 4). Table I summarizes this case.

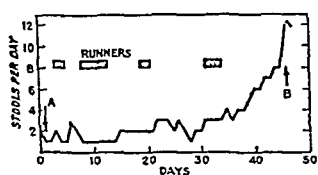


FIG. 1.

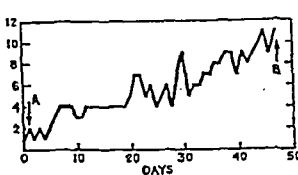


FIG. 2.

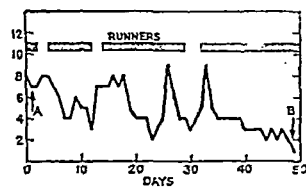


FIG. 3.

FIG. 1.—April 4, 1941: Relapse as runners became unobtainable. At A, feeling well, no pain, normal stools; weight 11 st. 12 lb. At B, pain, diarrhoea, blood and mucus in stools, lassitude; weight 11 st. 4 lb.

FIG. 2.—Nov. 7, 1942: Relapse when runners were discarded voluntarily. At A, feeling well and at work; no pain, normal stools. At B, too ill to work, easily tired; pain, diarrhoea, faecal incontinence, blood and mucus in stools.

FIG. 3.—Jan. 30, 1943: Slow improvement when taking runners. At A, off work; pain, lassitude, blood in stools. At B, feeling well and working overtime; no pain, normal formed stools.

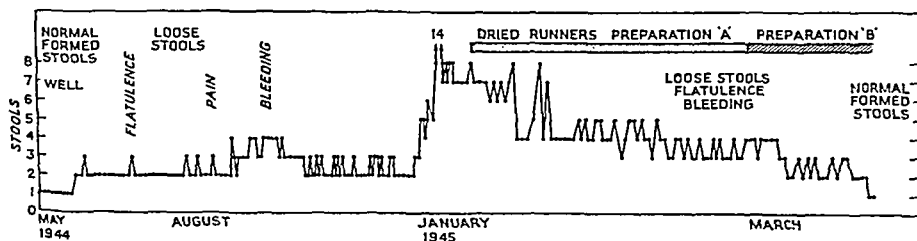


FIG. 4.—Course of Case I. From May, 1944 to January, 1945, each dot represents two days; thereafter each dot represents one day.

Acknowledgments: Figs. 1, 2 and 3 appeared in *Lancet*, 1944 (i), 536, and fig. 4 in *Lancet*, 1945 (ii), 203.

During the war I saw few cases of ulcerative colitis. Table II tabulates these, showing a response to raw pig's small intestine in 3 cases, no improvement in 2.

Of 3 further cases treated with preparation A, none showed material improvement. Of 12 further cases treated with preparation B, 8 became completely well and have

X-ray of skull shows a deep pituitary fossa, which is normal in size.

All urinary investigations were normal. Volume of urine 1,360 c.c. per day. 17-ketosteroids 3.3 mg. per litre or 4.5 mg. per day.

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Testicular biopsy: Marked atrophy of seminiferous tubules and great hyperplasia of interstitial cells.

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such a serious problem. He had always been impressed by the similarity of acute ulcerative colitis to mercurial poisoning as if the process consisted of eliminating some toxic product from the mucosa.

Dr. F. Avery Jones suggested that new treatments for colitis would have good results if given with enthusiasm. The patient with this chronic illness was particularly susceptible to emotional factors. This made the assessment of new remedies particularly difficult and it was important to have a control series using some similar but presumably inert preparation.

Dr. W. A. Oliver said that he had had a recent experience of a case of ulcerative colitis with a bad relapse lasting seven months, who failed to show any improvement with rest in bed and conservative treatment, but who responded dramatically following enthusiastic treatment with "Pepsac" (hog's stomach). Perhaps this would be an example of the control treatment with an inert powder suggested by Dr. Avery Jones.

Some Observations on the *Ætiology* and Treatment of Sprue

By A. L. WINGFIELD, M.D.

THE main features of tropical sprue are flatulent dyspepsia with abdominal distension and frequent bulky, pale, frothy and fatty stools. Cheilosis, glossitis, anæmia, and gross emaciation may be regarded as important but secondary manifestations. Clinically the primary dysfunction is a failure of intestinal absorption, while the secondary features result from deficiency of vitamins, foodstuff, or hæmatinic principle.

Of the morbid anatomy very little is known. The classical descriptions of atrophy and dehydration of all the main viscera and of the intestines are entirely correct but apply only to extreme cases with fatal issue. Practically nothing is known of the gross anatomical or of the histological changes in the earlier stages, but the very rapid response to correct treatment leads to the supposition that no serious change of structure occurs until the disease is far advanced, and Stannus has said that there are no early pathological changes. It is unlikely that much progress will be made in this direction as there is no real occasion, or should one say excuse, for biopsy observation, and death from intercurrent conditions is uncommon. It is not possible to produce the syndrome in experimental animals.

In the matter of *ætiology* some progress is being made. Infection is thought to play a definite part and the evidence for this cited by Galloway (1905) was reinforced by Manson-Bahr (1915) and more recently by Leishman (1945), but convincing proof is still lacking. The importance of vitamin deficiency is evidenced by the cheilosis, glossitis, and by the response to treatment. Stannus (1942) showed that failure of phosphorylation might account for the faulty absorption of fat and of glucose, while Leishman (1945) has elaborated this interesting theory by suggesting that nicotinic acid and riboflavin, which occur in the body in phosphorylated form, are able to catalyse phosphorylation and that the process of intestinal bio-synthesis of vitamins is subject to gross interference by an infective agent. The relationship of sprue to pellagra is entirely fortuitous and there is no common *ætiological* factor. Chronic jejuno-ileal insufficiency as suggested by Bennett and Hardwick (1940) has a superficial attraction but does not help in elucidating the *ætiology*. Hurst (1942) put forward a theory that paralysis of the muscularis mucosæ leads to a loss of the pumping action of the villæ, but there is no acceptable evidence to support this suggestion. Radiological abnormalities have been much discussed but they require highly specialized interpretation and do not help either in elucidating the cause or in giving guidance as to correct treatment. The occurrence of macrocytic anæmia, even in the presence of gastric hydrochloric acid, suggests a failure of absorption of hæmatinic principle from the intestinal tract rather than a failure of production by the gastric mucosa. If it can be accepted that anæmia is a result only of failure of intestinal absorption of hæmatinic principle, Manson-Bahr's (1941) and de Langen and Lichenstein's (1936) recognition of the many parallel features of sprue and pernicious anæmia lose some of their significance, and the similarity of the two conditions becomes logical. Present evidence seems to point to a failure of the intestinal mucosa to perform its normal function of absorption and, if this one assumption proves to be correct, all the clinical manifestations of the syndrome are to be regarded as the direct result of this one derangement. The very rapid response to treatment points strongly to a disorder of function rather than of structure, but, for the time being, most of our ideas about the *ætiology* of this syndrome are based upon clinical observation unsupported by controlled experiment.

Stannus says: "There is a functional derangement of the bowel due to deficient fat absorption and not deficient fat absorption due to paralysis of the muscularis mucosæ of its wall."

This aspect requires further detailed investigation which should include comparative analysis of food intake and fæcal output, and experiment to demonstrate, if possible, the

remained so, relapsing on ceasing treatment, regaining health on re-starting the extract (Table III).

In conclusion I would make the following points:

(1) That the term ulcerative colitis covers more than one disease, or, alternatively, that the aetiology of all cases of ulcerative colitis is not the same.

(2) That in one group of cases the cause may lie in some deficiency caused by a lack of some factor produced by the small intestine. Treatment of some cases of ulcerative colitis with intestinal mucosa has given promising results.

(3) Increasing the dose of desiccated mucosa beyond 1 oz. (= ½ lb. raw material) daily produces no better results. On the other hand, a small dose (e.g. 1 drachm daily)

TABLE I—SUMMARY OF CASE 1.

3 years' continuous symptoms. 1 year routine treatment—no improvement

3 months' ox stomach—no improvement

{ 6 weeks' pig's stomach and intestine—recovery

{ 3 months' pig's intestine only—remained well

Treatment stopped—gradual relapse

{ 4 weeks' pig's intestine—recovery

{ 3 months' pig's intestine—remained well

Supplies failed—relapse for 1 year

{ 4 weeks' pig's intestine—recovery

{ 6 months' pig's intestine—remained well

Treatment stopped—relapse

{ Pig's intestine resumed—recovery

{ Pig's intestine for 1 year—remained well

Treatment stopped—relapse

Dried preparation A—partial recovery

Dried preparation B—full recovery

TABLE II—TREATMENT WITH PIG'S SMALL INTESTINE.

Age	Sex	Duration of illness	Treatment	Result
21	M	3 weeks	(1) S. guanidine (2) Runners for 3 wks.	(1) Nil (2) Became well
26	F	6 years. Present relapse 3 weeks	(1) S. guanidine (2) Runners for 3 wks.	(1) Nil (2) Became well
35	M	1 year	Runners for 4 weeks	Became well
24	M	2 weeks	S. guanidine Runners Blood transfusions	Nil Died of perforation of colon
29	M	6 months	S. guanidine Runners Blood transfusions	Nil

TABLE III.—TREATMENT WITH ORAL DESICCATED DEFATTED INTESTINAL MUCOSA.

Age	Sex	Duration of illness	Treatment	Result	Age	Sex	Duration of illness	Treatment	Result
35	F	2 years. Present relapse 4 months	1 oz. (equiv. to ½ lb. fresh material) daily preparation A for 8 weeks	Improved but not cured. (Stools fell from 12 to 4 daily)	23	M	7 years	(1) S. guanidine (2) Preparation B for 6 weeks	(1) No improvement. (2) Improved but not cured
33	M	8 years. Present relapse 4 months	1 oz. daily preparation A for 8 weeks	Improved. (Stools fell from 8 to 4 daily)	29	F	4 years	Preparation B for 2 months	Improved but not cured
40	F	2 years	1 oz. daily preparation A for 6 weeks	Nil	38	F	17 years	Preparation B for 2 months	Well
50	F	1 year	(1) S. guanidine (2) 1 oz. daily preparation B for 4 weeks	(1) S. guanidine induced a remission on 2 occasions and then became ineffective. (2) Further complete remissions have followed prep. B	16	M	2 years	(1) S. suxidine (2) Preparation B for 6 weeks	(1) Induced a remission at first and then became ineffective. (2) Became well
31	M	1 year	1 oz. daily preparation B for 6 weeks	Became well	30	F	3 years	Preparation B for 4 weeks	Well
50	M	3 months	1 oz. daily preparation B	Died after 10 days with perforation of colon	25	M	4 months	Preparation B for 4 weeks	Well
47	M	6 months	(1) S. guanidine (2) 1 oz. daily preparation B for 4 weeks	(1) Remission induced. Then became ineffective. (2) Became well	40	F	10 years	Preparation B for 8 weeks	No improvement. Ileostomy
					27	F	4 years	Preparation B for 6 weeks	Well

is without effect. In all cases there is a latent interval of about three weeks before any appreciable improvement is noted.

(4) Mucosa taken from the different anatomical segments of the small intestine seems to be effective, although possibly jejunal mucosa produces a more lasting effect.

(5) A new highly concentrated preparation (Allen and Hanbury) is now on trial. 1 drachm = 1 oz. of preparation B. It has so far been given to a small number of patients.

(6) The mode of action of this form of therapy is still unproven.

Sir Philip Manson-Bahr said that the proposition of Dr. Morton Gill was an attractive one, and it had always seemed to him that ulcerative colitis was due rather to some inbred cause than to an extraneous infection. But he was doubtful whether this method of treatment had any effect upon those extremely toxic fulminating cases that presented

such a serious problem. He had always been impressed by the similarity of acute ulcerative colitis to mercurial poisoning as if the process consisted of eliminating some toxic product from the mucosa.

Dr. F. Avery Jones suggested that new treatments for colitis would have good results if given with enthusiasm. The patient with this chronic illness was particularly susceptible to emotional factors. This made the assessment of new remedies particularly difficult and it was important to have a control series using some similar but presumably inert preparation.

Dr. W. A. Oliver said that he had had a recent experience of a case of ulcerative colitis with a bad relapse lasting seven months, who failed to show any improvement with rest in bed and conservative treatment, but who responded dramatically following enthusiastic treatment with "Pepsac" (hog's stomach). Perhaps this would be an example of the control treatment with an inert powder suggested by Dr. Avery Jones.

Some Observations on the *Ætiology* and Treatment of Sprue

By A. L. WINGFIELD, M.D.

THE main features of tropical sprue are flatulent dyspepsia with abdominal distension and frequent bulky, pale, frothy and fatty stools. Cheilosis, glossitis, anæmia, and gross emaciation may be regarded as important but secondary manifestations. Clinically the primary dysfunction is a failure of intestinal absorption, while the secondary features result from deficiency of vitamins, foodstuff, or hæmatinic principle.

Of the morbid anatomy very little is known. The classical descriptions of atrophy and dehydration of all the main viscera and of the intestines are entirely correct but apply only to extreme cases with fatal issue. Practically nothing is known of the gross anatomical or of the histological changes in the earlier stages, but the very rapid response to correct treatment leads to the supposition that no serious change of structure occurs until the disease is far advanced, and Stannus has said that there are no early pathological changes. It is unlikely that much progress will be made in this direction as there is no real occasion, or should one say excuse, for biopsy observation, and death from intercurrent conditions is uncommon. It is not possible to produce the syndrome in experimental animals.

In the matter of *ætiology* some progress is being made. Infection is thought to play a definite part and the evidence for this cited by Galloway (1905) was reinforced by Manson-Bahr (1915) and more recently by Leishman (1945), but convincing proof is still lacking. The importance of vitamin deficiency is evidenced by the cheilosis, glossitis, and by the response to treatment. Stannus (1942) showed that failure of phosphorylation might account for the faulty absorption of fat and of glucose, while Leishman (1945) has elaborated this interesting theory by suggesting that nicotinic acid and riboflavin, which occur in the body in phosphorylated form, are able to catalyse phosphorylation and that the process of intestinal bio-synthesis of vitamins is subject to gross interference by an infective agent. The relationship of sprue to pellagra is entirely fortuitous and there is no common *ætiological* factor. Chronic jejuno-ileal insufficiency as suggested by Bennett and Hardwick (1940) has a superficial attraction but does not help in elucidating the *ætiology*. Hurst (1942) put forward a theory that paralysis of the muscularis mucosæ leads to a loss of the pumping action of the villæ, but there is no acceptable evidence to support this suggestion. Radiological abnormalities have been much discussed but they require highly specialized interpretation and do not help either in elucidating the cause or in giving guidance as to correct treatment. The occurrence of macrocytic anæmia, even in the presence of gastric hydrochloric acid, suggests a failure of absorption of hæmatinic principle from the intestinal tract rather than a failure of production by the gastric mucosa. If it can be accepted that anæmia is a result only of failure of intestinal absorption of hæmatinic principle, Manson-Bahr's (1941) and de Langen and Lichenstein's (1936) recognition of the many parallel features of sprue and pernicious anæmia lose some of their significance, and the similarity of the two conditions becomes logical. Present evidence seems to point to a failure of the intestinal mucosa to perform its normal function of absorption and, if this one assumption proves to be correct, all the clinical manifestations of the syndrome are to be regarded as the direct result of this one derangement. The very rapid response to treatment points strongly to a disorder of function rather than of structure, but, for the time being, most of our ideas about the *ætiology* of this syndrome are based upon clinical observation unsupported by controlled experiment.

Stannus says: "There is a functional derangement of the bowel due to deficient fat absorption and not deficient fat absorption due to paralysis of the muscularis mucosæ of its wall."

This aspect requires further detailed investigation which should include comparative analysis of food intake and faecal output, and experiment to demonstrate, if possible, the

response of individual manifestations of deficiency to specific therapy. The low blood sugar curve is said by Thaysen (1929) to be due to some cause other than deficient absorption but further work on this aspect of the problem is required, and Thaysen's view may prove to be incorrect.

Response to treatment with certain liver extracts supports the probability of a factor of deficiency while the occurrence of sprue in minor local epidemics gives colour to the possibility of an infective agent. The great variety of diets advised in years gone by leads to the almost inescapable conclusion that none of them had any specific virtue and that all of them owed their partial success to a reduction of the fat content of the diet or simply to a reduction of bulk. Certain of the diets have a high vitamin content and in ancient times the Chinese already employed liver in the treatment of sprue.

Nevertheless, vitamins, when given by mouth, have no therapeutic effect and I have frequently observed that the largest doses of nicotinic acid are tolerated without either vasomotor or digestive disturbance on the one hand, or clinical improvement on the other. It is improbable that any of the diets formerly employed had any vitamin content of specific value in this syndrome, until intestinal absorption was restored to normal.

Treatment.—Keele and Bound (1946) writing from the Sprue Research Team, Poona, describe their treatment, which was designed only to make the patient fit to travel, under the following headings:

(1) Diet: The high protein, low fat, low carbohydrate diet of Fairley (1930, 1936) was adopted. A series of five diets compiled by Napier (1943) was used as a basis. The importance of constancy and regularity of diet was emphasized and increase was often followed by relapse. Nicotinic acid and sometimes riboflavine were added.

(2) Bed rest: This they regard as important.

(3) Parenteral liver they regard as unnecessary in most mild cases but "useful" in all severe cases.

I have quoted this recent paper as being, perhaps, typical of current opinion in this country but I would hasten to add that my own views are very different.

Rhoads and Miller (1934) and Castle and co-workers (1935) showed that the anaemia and other symptoms of sprue all respond to liver when given as a crude extract parenterally. This observation has been proved beyond any doubt and should be the basis of all modern treatment of this syndrome.

In 1939 there came under my care a merchant captain with the fully developed syndrome of sprue together with severe macrocytic anaemia. He was treated with high protein, low fat diet and large doses of anahæmin which is generally accepted as a liver extract of high anti-anaemic potency. The patient's blood picture made a rapid improvement but his general condition deteriorated and he died after about five weeks in hospital. Autopsy showed the classical picture of dehydration with visceral and intestinal atrophy.

Death from sprue is by no means uncommon in spite of a satisfactory blood picture and Manson-Bahr (1915) in his admirable monograph was already able to quote two such cases.

This single misfortune did something to destroy my belief in the value of diet and caused me to reconsider the place of parenteral liver therapy.

The next patient to come under my care was aged 70 and had had a previous attack of sprue two and a half years before with spontaneous remission. The stools were typical but her general condition was good. She had severe macrocytic anaemia. She was treated with intramuscular injections of Hapatex T and both her stools and blood picture quickly returned to normal although she continued to take full ward diet without any restrictions.

Since that time it has been my practice to allow all patients with sprue to take a full ward diet, and to get up when they wish. They receive crude liver injections in the form of Plexan 4 c.c. daily for one week, alternate daily for one week and twice weekly thereafter, and to this is added oral nicotinic acid 50 mg. t.d.s.

A single dose of nicotinic acid 150 mg. is given to test vasomotor and digestive reactions. So far no patient tested has complained of flushing before the beginning of treatment, while all patients have given a specific vasomotor response after treatment for two to three weeks. This observation supports the contention that crude liver quickly restores intestinal function. Nine consecutive patients have been treated in this way and the response in every case has been satisfactory. The average gain in weight has been 27 lb., varying from 13 lb. to 52 lb. Stools return to normal in about seven days and the only untoward phenomena have been pain at the site of injection and a transient oedema of the feet and legs, which generally appears in the second week, and may be due to sodium retention. Only one patient has relapsed and this only for a few weeks. Dr. Wilfrid Oakley has treated two patients in the same way. The

first, aged 29, gained 35 lb. in two months, while the second gained 31 lb. in four months and when last seen was a little troubled by constipation.

One patient similarly treated by another colleague has gained 29 lb. in five weeks with return of normal bowel function.

Two of my own patients call for particular comment. The first, a lady aged 51, recently home from India, presented the full syndrome of sprue with severe emaciation, and weighed only 74 lb. She had been on a fat-free diet and had had injections of liver of an unspecified brand.

She had only a moderate degree of anaemia. In October 1945 she was admitted and given the treatment already described of normal ward diet with injections of Plexan. Her weight to-day is 135 lb. or almost doubled. Figs. 1 and 2 are photographs of this patient taken before and after treatment.



November 4, 1945

FIG. 1.



April 2, 1946

FIG. 2.

The second patient on whom I should like to comment in more detail was first seen with the full syndrome by a colleague. He was treated with diet, vitamins by mouth and injections of Hepatex T. He was transferred to my care because his weight had not increased very much, and glossitis, cheilosis, and some looseness of the bowels had persisted. Oral nicotinic acid produced no reaction. He was then treated according to our present routine. The glossitis and cheilosis disappeared within a week, his moderate anaemia disappeared and he gained 9 lb. in weight in three weeks. After fourteen days, flushing occurred with 150 mg. of nicotinic acid.

The response of this small series of patients to crude liver injections has caused me to believe that diet is of little or no consequence in the treatment of sprue. It seems that there is a deficiency due to a functional disorder of intestinal absorption which can only be remedied by adequate parenteral therapy. With only two exceptions these patients have remained under prolonged observation, and in only one case has relapse occurred.

The response to Plexan may not be specific and I wish to imply no criticism of other branded liver extracts. Nevertheless it is highly probable that Plexan contains "impurities" which are of the highest value in the treatment of sprue. The next step must obviously be to try to identify the nature of the "impurity".

The active constituent contained in liver extract is not known but a plan has been devised which may eventually lead to its isolation, provided that patients become available for the work. It is possible that after heavy initial doses smaller and less frequent injections may prove sufficient for maintenance, and trial of this is now proceeding.

Comment.—I believe that there is now sufficient evidence to show that sprue is a deficiency disease possibly resulting in the first place from an intestinal infection. The subsequent course is conditioned by a functional disorder of the bowel which interferes with absorption of fat, carbohydrate and a hypothetical essential factor. Certain crude liver extracts contain a substance which restores the function of the bowel, and at the same time either permits vitamin absorption from the intestine by the process of phosphorylation or itself provides the missing factors.

The various fractions of the vitamin B₁₂ complex have been used at different times, both orally and parenterally. It is improbable that any of them have any specific

value in this syndrome, although their combined parenteral administration might be useful. Nevertheless crude liver is a potent source of vitamin B₂ complex and it is possible that an unidentified fraction may prove to be the specific factor. The search for this "S" factor must start from those crude liver extracts which undoubtedly contain it, and will not be complete until it has been chemically identified. At the present time only Plexan has given consistent therapeutic response in my hands but others are no doubt effective as in one of my cases treated with Hepatex T.

If these assumptions are correct planned research should lead to the isolation of the essential factor.

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Sir Philip Manson-Bahr agreed entirely with Dr. Wingfield that liver injections afforded the best means of treating tropical sprue. The cruder the preparation the better; the most favourable results had been obtained with the Bayer product of Campolon, but since the war, with Plexan which was a similar preparation. Furthermore he agreed that large continuous dosage was necessary. For controlling the diarrhoea in the earlier stages of treatment he had recently used sulphaguanidine or sulphasuxidine in 10 to 12 grammes daily doses. He agreed that the appearance of the nicotinic acid reaction was probably a good indication of the restoration of normal absorption from the small intestine. It would undoubtedly be desirable to make further observations on this point.

Dr. H.-S. Stannus said that Dr. Wingfield, by emphasizing the importance of dosage in the treatment of sprue by crude liver extracts, had performed a valuable service. The treatment by large doses is not new, as he had stated, but the point had not always been recognized in the past and might be overlooked by younger men called upon to treat the disease.

Ideas concerning treatment should be bound up with ideas concerning pathogeny. Writing in 1942 he (Dr. Stannus) had brought forward evidence for believing that the failure in sprue lay primarily in deficient phosphorylation of fatty acids, the absorption of neutral fats being interfered with secondarily to a greater or less extent. In the latter case wasting is not a pronounced feature as in one of Dr. Wingfield's cases. The absorption of neutral fats and of fatty acids according to the "partition" theory of Alastair Frazer occurs by different methods, the two follow different paths with different destinations. This theory Dr. Stannus applied to sprue. Fatty acids are phosphorylated with the formation of phospholipids before absorption takes place, neutral fats are absorbed as a fine emulsion. One believes that in crude liver extract there is a factor which like other vitamins acts as a co-enzyme—united to a specific protein, the apoenzyme, it catalyses the phosphorylation of fatty acids in the bowel.

Wing Commander J. W. Paulley said that he had had the opportunity for a period of eighteen months of receiving cases of sprue invalided from the Eastern theatre of war. Efforts had been made at a careful analysis of these cases, and one of the most notable features of this analysis had been figures of preceding intestinal infection at a rate approximating to Sir Philip Manson-Bahr's figure of 40-5% but being higher than the published figures of Leishman, and those of Keele and Bound.

Working in conjunction with Squadron Leader G. J. Aitken he had carried out nicotina-mide methochloride excretion tests in a small series of controls, of sprue, convalescent sprue and amoebiasis. The method used was that of Coulson, Ellinger and Holden (*Biochem. J.*, 1944, 38, ii, 150), and of Ellinger Benesch and Hardwick (*Lancet*, 1945 (ii), 197). The result of these investigations showed, as far as they went, a deficient excretion in cases of sprue, even though the latter had been totally free of symptoms for three months or more, and also in amoebiasis, though the majority of the latter were not suffering from intestinal "hurry".

He mentioned these rather unexpected, though unconfirmed findings, in the discussion for what they were worth.

Dr. W. E. Cooke said that recently he had sent a patient to Dr. Wingfield who had only improved slowly on Hepatex but whose improvement on Plexan was remarkable.

Dr. Wingfield's statement that patients with sprue were put on full ward diet on admission to hospital was a practice that was not free from danger for in some patients perforation might occur. Sir Philip Manson-Bahr would concur with him that they had seen this happen.

Dr. Wingfield (in reply): I am glad to find so large a measure of agreement as to the need for large doses of crude liver. It is to be hoped that this treatment will be generally employed. The possible dangers of full diet are appreciated and in several emaciated patients a few days of milk and egg diet is needed before progress to unrestricted dietary is ordered.

Section of Laryngology

President—G. EWART MARTIN, F.R.C.S.Ed.

[May 3, 1946]

DISCUSSION ON RHINOLOGY IN THE MEDITERRANEAN AND AFRICAN AREAS

J. P. Stewart: I was responsible for the ear, nose and throat work in a British General Hospital at Teheran during 1943 and it was from that source that the material for this paper comes. The climatic and hygienic conditions are so intimately bound up with the infection of the paranasal sinuses, that I will briefly outline their main features. The southern half of Persia is mostly composed of arid barren desert. The summers are very hot with hardly a cloud visible in the sky and with a temperature of as much as 130° F., while the winters, though of short duration, are very cold with a temperature just above freezing point or even below zero. The rainfall is scanty even in winter. The annual fall in Teheran is 9.53 inches, so that the humidity is exceedingly low. For four months in the summer a constant dust-laden wind, which is called the Shamal, blows from the North West. Whirlwinds wherein columns of dense dust and small stones are caught up, and going by the name of "dust devils" or "whirligigs", suddenly arise and tear through space drenching with dust everything and everybody in their erratic course. Sanitation is extremely rudimentary and much of the human excreta is deposited in open spaces. The sun bakes the excreta and in a very short space of time it disintegrates, becomes pulverized, and is blown about in the dust. There is no piped water from reservoirs and the water supply is obtained from open streams and if I describe the water supply of the capital city, Teheran, it will give an idea of the primitive conditions of such a supply. The main water supply is derived from the streams which run down from a mountain range some 10 miles distant and those streams often pass through some small villages in their course. Short of the city these streams are directed into open artificial channels and then led into the city to be diverted into large gutters with an earth or cement base which run down the principal streets. One does not need a great stretch of imagination to visualize the indignities to which this water supply is subjected to during its course through the city. Swimming pools were filled from the open supply but the water was taken off from as far out from the city as possible and they were, when under military supervision, heavily chlorinated. Despite the heavy chlorination many cases of paranasal sinus infection arose from these swimming pools as no doubt the heat of the water and the exceptional number of people using the pool contributed in no small measure to the infectivity obtaining in it. In the field, water was scarce and the best of it was taken for drinking purposes so that practically any other source of supply was used for washing. The British Tommy when washing invariably threw handfuls of water on to his face some of which would enter the nasal cavities and it was quite a common practice for him to sniff water into the nose and then expectorate it as this moistened his dry nose and washed the dust and grit out of it. It can readily be appreciated that infection of the nasal cavities might thus take place by the introduction of infected water.

Locomotion was by motor transport and a column on the move was shrouded in a thick dust pall which coated the individual from head to foot and irritated the upper air passages beyond measure, and one's expectoration was black with grit and dust.

During the ten months 896 ear, nose and throat cases passed through my Department and 303 suffered from an affection of the external or internal nose. 154 (51%) of those cases were due to an infection of one or other of the paranasal sinuses. The maxillary air sinuses were affected either uni- or bilaterally in 106 cases, the frontal sinuses

similarly in 8 cases, and a combination of these two sinuses in 8 cases, the ethmoid cells in 30 cases and a pansinusitis occurred in 2 cases. A preliminary X-ray examination of the sinuses was made in every case, and a proof puncture was performed to confirm the radiological findings in cases of suspected maxillary antrum infection. In 40 cases the returning fluid from the antral wash-out was clear or had shreds of mucus in it but there was a varying amount of resistance to the irrigating fluid thus demonstrating a swollen antral mucosal lining. A further 21 cases yielded mucopus while in 54 cases frank pus was washed out, generally in copious quantity.

This high incidence of every second case suffering from nasal sinus disease was mainly due to climatic and hygienic factors. The intense heat of very low humidity dried up the natural secretions of the nasal mucosa causing the mucous membrane to become congested, dry and glazed. Infected dust was then inhaled, which impregnated this irritable membrane thus opening up the pathways of infection. When infection became established and an exudate formed, it too was dried up and formed a cake or crust which retarded further drainage from the deeper structures and in fact sealed them off. Much the same sequence of events was produced by infection which was water-borne though dust was by far the most frequent infecting agent. A number of cases gave a history of a previous attack of nasal sinusitis which, though it had cleared up, recurred readily under the conditions described.

The treatment of those cases of nasal sinus disease, which took place in the penicillin era, did not differ from that employed elsewhere. There was little contra-indication to operation but one had to be on the outlook for signs of heatstroke and heat exhaustion especially if there was much loss of blood, post-anæsthetic vomiting, or indeed any marked dehydration of the tissues. If the patient had suffered from a previous attack of malaria, operation often precipitated another attack giving rise to a high temperature which was rather worrying until the cause of it was ascertained, therefore a blood slide was taken as a routine from all cases which ran a temperature following operation. 42 cases were operated upon—31 radical antrum operations, 1 intranasal antrum drainage, 4 external frontal sinus, 1 intranasal frontal sinus drainage and 5 ethmoidectomies were performed.

The post-operative results were rather disappointing but I believe that if penicillin had been available those results would have been much more satisfactory. The sulphonamides did not prove of great value in promoting healing. Recovery was retarded mainly because of a constant reinfection of the raw areas. The operation cavities continued to suppurate for a long time so that it became necessary to advise, in the majority of cases, evacuation to a more equable climate.

In the course of time our experience taught us to operate less and less on this type of infection and any marked case of sinusitis was at once recommended for evacuation.

R. B. Lumsden (Abridged): Climate.—Except for a narrow belt along the Mediterranean shore, where 8 to 12 in. of rain falls in the winter months only, Egypt is almost rainless. At Alexandria, the mean maximum temperature is 99° F.; while 130 miles inland at Cairo, where the proximity of the desert begins to be felt, it is 110° F. At Cairo the mean relative humidity in summer is about 45% and in winter about 70% (Encycl. Brit.). There are periods, however, especially in spring, but also in autumn and summer, when this is much lower. These periods occur during the "khamsin"—a dusty, sand-laden wind which blows off the desert for several days on end, during which the temperature is high and the air extremely dry. These "khamsins" also occur in Palestine, where hot, dry summers are experienced, but where, unlike Egypt, there is a heavy winter rainfall.

Sinusitis.—During the year 1944, the total number of ear, nose and throat cases seen throughout the Command was 27,816, of which 6,105 (22%) were nasal cases. Of these, 834 (13.7%) were admitted to hospital on account of sinusitis; 347 (5.7%) being chronic and 487 (8%) acute (see Table). Unfortunately consolidated records do not provide

MIDDLE EAST FORCE, 1944 (ALL HOSPITALS).

Total number of ear, nose and throat out-patients	27,816
Total number of nasal cases	6,105
Total number of nasal cases	6,105
Total number of throat cases (excluding acute tonsillitis)	3,337
Total number of laryngeal cases	656
Negative examinations	2,627

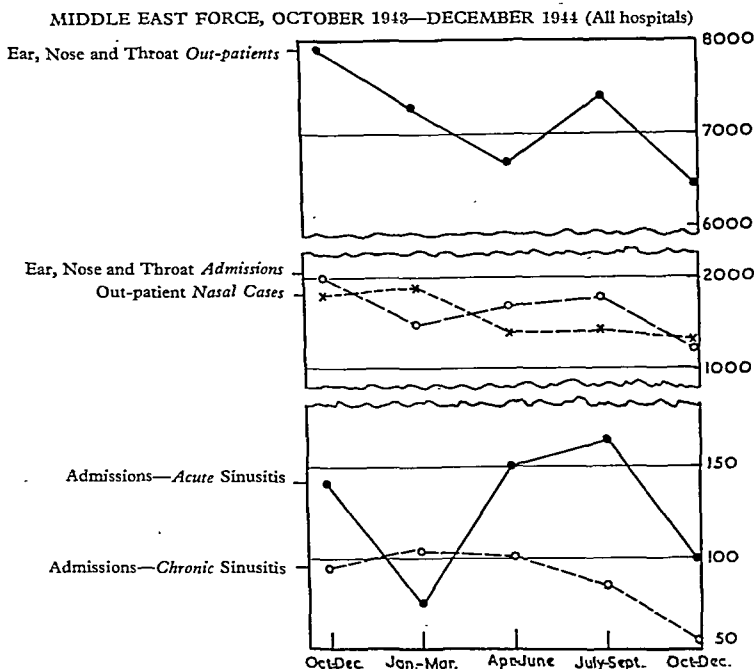
Cases admitted to hospital on account of sinusitis—	834	13.7% of all nasal cases
(a) Chronic	347	5.7% of all nasal cases
(b) Acute	487	8% of all nasal cases

figures relating to individual sinuses, nor do they afford any detailed statistical information concerning out-patient cases. Collins (1943), in Cairo, found that 20.3% of his total

out-patients and 66.8% of nasal cases suffered from sinus infection, but these figures appear to be high for the Middle East as a whole. Many of my own figures were unfortunately lost in transit.

Concerning *treatment*, Collins (1943) found that 74% of his sinus cases yielded to conservative measures, which included repeated proof puncture. There was general agreement with his plea for conservative methods. As after all nasal operations, convalescence was slower than at home and final operative results were, on the whole, less satisfactory. It appears that the penalties of interference with the nasal mucous membrane are infinitely greater in a hot, dry climate.

Seasonal incidence: At the top of the chart are shown the quarterly figures of (1) all ear, nose and throat out-patients, (2) out-patient nasal cases, and (3) ear, nose and throat hospital admissions throughout the Command; from October 1943 to December 1944. The general downward trends are an indication of a general reduction in the population. In the lower half of the chart the interrupted line shows the number of *admissions* to hospital on account of *chronic* sinusitis, and it will be observed that the seasonal incidence was fairly constant. The upper line relates to admissions on account of *acute* sinusitis and shows an appreciable summer rise. A similar incidence was observed in respect of less severe cases treated as out-patients.



Undoubtedly, many cases of sinusitis were related to swimming in fresh water pools (Collins, 1943; Lumsden, 1945); and resolution was generally slow. In South Iraq, on the other hand, Reeves (1943) comments on the small number of cases of acute sinusitis admitted during the dusty summer months. He found that the large majority occurred in the cold weather. It is to be noted that 48% of his patients were Indians.

There was general agreement with Collins (1943) concerning the frequency of frontal headache associated with sinus tenderness, and redness and frequently dryness of the mucosa of the middle turbinate. This condition occurs most frequently during the hot, dusty "khamsin" winds already mentioned and is most common in Egypt, where "khamsins" are associated with a much dustier atmosphere. As Collins has pointed out, while an allergic factor may be present, clinically it does not resemble vasomotor rhinitis. The diagnosis of acute frontal sinusitis was generally applied to these cases, but there would appear to be some justification for regarding the condition as that of "vacuum" sinus headache. Colleagues who served in different parts of the Middle East corroborate the opinion that this condition seldom occurs near the sea and Daggett informs me that

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This high incidence of every second case suffering from nasal sinus disease was mainly due to climatic and hygienic factors. The intense heat of very low humidity dried up the natural secretions of the nasal mucosa causing the mucous membrane to become congested, dry and glazed. Infected dust was then inhaled, which impregnated this irritable membrane thus opening up the pathways of infection. When infection became established and an exudate formed, it too was dried up and formed a cake or crust which retarded further drainage from the deeper structures and in fact sealed them off. Much the same sequence of events was produced by infection which was water-borne though dust was by far the most frequent infecting agent. A number of cases gave a history of a previous attack of nasal sinusitis which, though it had cleared up, recurred readily under the conditions described.

The treatment of those cases of nasal sinus disease, which took place in the penicillin era, did not differ from that employed elsewhere. There was little contra-indication to operation but one had to be on the outlook for signs of heatstroke and heat exhaustion especially if there was much loss of blood, post-anaesthetic vomiting, or indeed any marked dehydration of the tissues. If the patient had suffered from a previous attack of malaria, operation often precipitated another attack giving rise to a high temperature which was rather worrying until the cause of it was ascertained, therefore a blood slide was taken as a routine from all cases which ran a temperature following operation. 42 cases were operated upon—31 radical antrum operations, 1 intranasal antrum drainage, 4 external frontal sinus, 1 intranasal frontal sinus drainage and 5 ethmoidectomies were performed.

The post-operative results were rather disappointing but I believe that if penicillin had been available those results would have been much more satisfactory. The sulphonamides did not prove of great value in promoting healing. Recovery was retarded mainly because of a constant reinfection of the raw areas. The operation cavities continued to suppurate for a long time so that it became necessary to advise, in the majority of cases, evacuation to a more equable climate.

In the course of time our experience taught us to operate less and less on this type of infection and any marked case of sinusitis was at once recommended for evacuation.

R. B. Lumsden (Abridged): Climate.—Except for a narrow belt along the Mediterranean shore, where 8 to 12 in. of rain falls in the winter months only, Egypt is almost rainless. At Alexandria, the mean maximum temperature is 99° F.; while 130 miles inland at Cairo, where the proximity of the desert begins to be felt, it is 110° F. At Cairo the mean relative humidity in summer is about 45% and in winter about 70% (Encycl. Brit.). There are periods, however, especially in spring, but also in autumn and summer, when this is much lower. These periods occur during the "khamsin"—a dusty, sand-laden wind which blows off the desert for several days on end, during which the temperature is high and the air extremely dry. These "khamsins" also occur in Palestine, where hot, dry summers are experienced, but where, unlike Egypt, there is a heavy winter rainfall.

Sinusitis.—During the year 1944, the total number of ear, nose and throat cases seen throughout the Command was 27,816, of which 6,105 (22%) were nasal cases. Of these, 834 (13.7%) were admitted to hospital on account of sinusitis; 347 (5.7%) being chronic and 487 (8%) acute (see Table). Unfortunately consolidated records do not provide

MIDDLE EAST FORCE, 1944 (ALL HOSPITALS).

Total number of ear, nose and throat out-patients ...	27,816	
Total number of aural cases ...	15,091	54.3%
Total number of nasal cases ...	6,105	22%
Total number of throat cases (excluding acute tonsillitis) ...	3,337	12%
Total number of laryngeal cases ...	656	2.3%
Negative examinations ...	2,627	9.4%

Cases admitted to hospital on account of sinusitis—

(a) Chronic ...	347	13.7% of all nasal cases
(b) Acute ...	487	5.7% of all nasal cases
		8% of all nasal cases

figures relating to individual sinuses, nor do they afford any detailed statistical information concerning out-patient cases. Collins (1943), in Cairo, found that 20.3% of his total

tion, but I should guess I served upwards of 25,000. For the most part these men were engaged in clerical work, or in maintenance of supplies to the various theatres of war.

The contrast between my Service patients and the few natives I saw was striking. I think a laryngologist requires an educated patient, if he is to give of his best, but with the natives I saw it was obvious that no amount of explanation or of reason would be of use. They required a quick and dramatic form of treatment, and a promise of absolute cure.

In the last few months of my appointment I went to Palestine once a week to visit the R.A.F. Hospital near Tel Aviv. It is suggestive for the future that I began my clinic there at 9.30 in the morning, having already travelled 250 miles by air from Cairo. I returned to Cairo the same evening, having seen between 20 and 30 out-patients, and this I did regularly each week.

Cairo was a surprise to me, as I think it is to most Englishmen. It is an ancient city which has never been sacked, nor has it been destroyed by fire. The present city certainly dates back to the Romans and the streets are now some 40 ft. above the floor level of the old Coptic churches. There is no rain and the dust cloud is continuous, so much so that the sun never tans the skin in the city and the suburbs. Most of my patients were quartered in or near the city and I am sure the atmosphere was a cause of the infections of the nose and throat.

The desert was healthier and I was often told that symptoms of sinus infection were less troublesome there. The weather too had much to do with the number of cases seen, but it is easier to be sure of the weather as a factor, as infections varied so obviously with the seasons. The Nile rises in mid-June and it is at this time that cases of sinus infection are seen in greatest numbers.

In Cairo antral infection rises steadily to a peak in July, when we had to set aside two mornings for antral lavage alone. I will describe results of treatment later, but by the expression antral infection, I include all cases where the infection of the antrum is the controlling factor, although other sinuses may be involved.

I think antral infections are more common in the Services generally than they are amongst civilians and a possible reason is the fact that a number of people live and work in close contact. In Cairo, at all events, the outdoor bathing pools were responsible for a number of sinus infections. Everyone bathed in Cairo and bathing is possible for nine months in the year. The pools were used every day and in most cases all that could be done was to empty them, and chlorinate them overnight. They were, in fact, only empty for an hour or two during the night. So many patients came with a history which began after bathing, that it was obvious that there was some relation, but while it was clear that the swimming pools made the infection worse, it was still possible that the infection had already been planted in the nose.

These cases were admitted with the usual signs of an acute sinusitis. If they improved with rest and inhalations I did not wash the antrum out, but this was often necessary. If the infection was overcome in this way, there was no difficulty, but the chief problem was the subacute or recent case which did not improve.

However, an antral infection which has not improved with lavage and rest is not enough to justify repatriation, and it was my experience that transfer to another Middle East climate, such as Palestine, did little good. I think many would have recovered in England, but I could not send them home for this reason.

This will explain, I hope, the number of operations for acute and subacute sinusitis. Where the history was longer than six months, and there was no improvement after the antrum had been washed out six times, an antrostomy was performed. The results were fairly good; certainly equal to what I would expect in England.

It is curious that recovery from operation is as good in Cairo as it is in England, even in hot weather. There were few complications: the alveolar incision in a Caldwell-Luc antrostomy perhaps became more readily infected, and certainly closed more slowly, sometimes taking three months. The worst complication I saw was infection of the fat of the cheek following a Caldwell-Luc antrostomy, and subsequent slow separation of the slough. There was one death, in an officer who had a recent infection, and who was recommended for operation because he held a key position in the Middle East. He developed an acute pancreatitis, and later died from an empyema.

Two interesting cases were two young Australians, both referred with bronchiectasis and antral infection. Both these men had only been a few months in the Middle East, and had never had either sinus or chest symptoms before. After this, I looked carefully

he did not encounter such cases in Malta, where the climate remains humid throughout the year.

A series of laboratory experiments on rabbits has been carried out by Rosedale (1944) concerning effects of temperature and humidity on sinusitis. He found that a relatively cool and dry atmosphere was the most beneficial, while a hot and relatively dry atmosphere was the most harmful.

Though in several respects not strictly comparable, reports in recent literature suggest that the incidence of sinusitis is considerably higher in Egypt (Collins, 1943) than at home (Birrell, 1944), and that it is slightly higher at home than in North Africa (Birrell, 1944) and Iraq (Reeves, 1943).

Deviations of the septum: It was found, as in sinusitis, that patients who gave a history of mild symptoms of nasal obstruction at home frequently sought advice because these symptoms had become more marked and persistent after going abroad.

Atrophic rhinitis was encountered infrequently. Severe cases presumably were not sent overseas. The cases seen gave a history of relatively mild symptoms at home, but found summer conditions, especially in desert districts, quite intolerable and these had to be sent home.

In spite of the frequency and severity of *diphtheritic infections*—both faucial and cutaneous—nasal infection was very rarely encountered.

Leprosy was never seen in European Service personnel.

Nasal allergy.—True *pollen allergy* was judged to be comparatively uncommon and symptoms are of short duration. A number of people were encountered who suffered from hay fever at home, but did not experience seasonal symptoms in these regions. On the other hand, an appreciable proportion of the forces experienced mild symptoms of perennial *vasomotor rhinitis*. One frequently heard people commenting on their nasal stiffness and watery discharge, though only a relatively small proportion suffered enough inconvenience or discomfort to warrant seeking advice. Symptoms were accentuated during “khammins” and showed no appreciable tendency to diminish, even after long periods of residence, while, by way of contrast, it was observed that otitis externa took a much heavier toll of fresh arrivals than of those who were thoroughly acclimatized. Many of the severer cases gave a history of suffering from hay fever or mild perennial symptoms at home and these people were not prone to develop the dry nose with so-called “vacuum” sinus headache, so that an excessively moist nose affords a compensatory safeguard against this condition. The absence of this condition among African native troops was noted, though it occurs among the Egyptian population.

Finally, some advice concerning patients who propose to proceed to this part of the world:

(1) Sufferers from *nasal affections* need not be dissuaded from spending the winter in Egypt. On the other hand, they should be discouraged from believing that their condition will benefit materially therefrom.

(2) Sufferers from chronic or recurrent acute sinusitis should be advised against spending the spring, summer or autumn months in any of the Middle East countries.

(3) Persons afflicted with true *pollen allergy* may escape the acute discomfort of the hay fever season at home, but they cannot confidently expect to enjoy complete freedom from all nasal symptoms.

(4) *Vasomotor rhinitis* is unlikely to be relieved and might be aggravated.

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William McKenzie: I was posted to Cairo from India in June 1943. The war by that time had left Cairo behind, and the nearest battle front was 1,000 miles away. The only active combatants in my area were the few pilots who undertook the exceedingly dangerous duties of photographic reconnaissance. I do not think my work differed much from work in peacetime in the Cairo area, if allowances are made for the greater likelihood of the spread of infection in barracks: there were of course large numbers of the Royal Air Force in the area; how many I never found out, as this was secret informa-

tion, but I should guess I served upwards of 25,000. For the most part these men were engaged in clerical work, or in maintenance of supplies to the various theatres of war.

The contrast between my Service patients and the few natives I saw was striking. I think a laryngologist requires an educated patient, if he is to give of his best, but with the natives I saw it was obvious that no amount of explanation or of reason would be of use. They required a quick and dramatic form of treatment, and a promise of absolute cure.

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The desert was healthier and I was often told that symptoms of sinus infection were less troublesome there. The weather too had much to do with the number of cases seen, but it is easier to be sure of the weather as a factor, as infections varied so obviously with the seasons. The Nile rises in mid-June and it is at this time that cases of sinus infection are seen in greatest numbers.

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I think antral infections are more common in the Services generally than they are amongst civilians and a possible reason is the fact that a number of people live and work in close contact. In Cairo, at all events, the outdoor bathing pools were responsible for a number of sinus infections. Everyone bathed in Cairo and bathing is possible for nine months in the year. The pools were used every day and in most cases all that could be done was to empty them, and chlorinate them overnight. They were, in fact, only empty for an hour or two during the night. So many patients came with a history which began after bathing, that it was obvious that there was some relation, but while it was clear that the swimming pools made the infection worse, it was still possible that the infection had already been planted in the nose.

These cases were admitted with the usual signs of an acute sinusitis. If they improved with rest and inhalations I did not wash the antrum out, but this was often necessary. If the infection was overcome in this way, there was no difficulty, but the chief problem was the subacute or recent case which did not improve.

However, an antral infection which has not improved with lavage and rest is not enough to justify repatriation, and it was my experience that transfer to another Middle East climate, such as Palestine, did little good. I think many would have recovered in England, but I could not send them home for this reason.

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It is curious that recovery from operation is as good in Cairo as it is in England, even in hot weather. There were few complications: the alveolar incision in a Caldwell-Luc antrostomy perhaps became more readily infected, and certainly closed more slowly, sometimes taking three months. The worst complication I saw was infection of the fat of the cheek following a Caldwell-Luc antrostomy, and subsequent slow separation of the slough. There was one death, in an officer who had a recent infection, and who was recommended for operation because he held a key position in the Middle East. He developed an acute pancreatitis, and later died from an empyema.

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for evidence of bronchiectasis as a complication of sinus infection in Cairo, but with no result.

If antral infection is common in Cairo, there is one condition which is rare compared with civilian life, and that is vasomotor rhinitis or vagotonia. I can say definitely that this condition was seldom seen compared with the incidence in a London clinic to-day.

Table I gives the numbers of cases of antral infection seen in Cairo, and the result of treatment.

Operation was of course only undertaken after failure of lavage, and in the acute and recent cases both lavage and operation were avoided.

A comparison with infections in Palestine is given in Table II. The number of patients is less altogether, but the danger from bathing was less, as it was scabathing for the most part. There is an increase, however, compared with England, and this I think must be due to the climate of the Mediterranean area generally.

TABLE I.—CAIRO No. 5 R.A.F. HOSPITAL.
July—December 1943.

Out-patients	869	Chronic					
Acute sinusitis	85	Improvement:	Rest and inhalation	2			
Chronic sinusitis	118		Lavage	23			
			Operation	34			
Results of treatment of antral infection							
<i>Acute and subacute</i>							
Improvement:		No improvement:	Lavage	5			
Rest and inhalation	20		Operation	10			
Lavage	34			19			
Operation	10		Secondary to swimming	6			
			Antral infection of dental origin	1			
No improvement:			Antral infection following gunshot wound	35			
Lavage	11		Allergic rhinitis	6			
Operation	1		Allergic rhinitis worse in Cairo				

TABLE II.—PALESTINE No. 3 R.A.F. HOSPITAL.
June—December 1944.

Out-patients	388	Chronic					
Infection of nasal sinuses... ..	70	Improved:	Lavage... ..	0			
Antral infection:			Operation	10			
<i>Acute and Subacute</i>				3			
Improved:		Not improved:	Lavage	1			
Lavage	19		Operation	2			
Operation	3		Secondary to swimming	1			
Not improved:			Antral infection of dental origin	1			
Lavage	2		Allergic rhinitis				
Operation	1						

R. Scott Stevenson spoke of his experience on Gibraltar, where he found a large amount of vasomotor rhinitis in people coming out from England who encountered a completely new flora with new pollens. About two hundred W.R.N.S. were working there, many in tunnels which were driven from one side of the Rock to the other, and among these a good deal of nasal trouble was found, owing to the prevalence of limestone dust. He employed desensitization by Francis's method of the irritable nasal mucosa, which in most of the cases gave a great deal of relief. One girl never left off sneezing as long as she was working in the tunnel, and her trouble in this respect was so severe that she was actually going to be sent back to England because of persistent rhinitis; repeated treatment with the dull-red galvano-cautery, however, enabled her to stay on at Gibraltar. The climate of Gibraltar was good, and during the two years he was there no rain fell from May until late September, but during the actual rainy season in March and April the fall was heavy; the annual rainfall was from 25 to 35 inches. There was a double water supply on Gibraltar, fresh and salt, the use of fresh water being much restricted. All their bathing was in the sea, and he did not believe that sea-bathing made sinusitis any worse; he had found many more cases of sinusitis when stationed in the West of Scotland, where it was very wet; he could remember seeing ten or a dozen cases in his out-patient clinic there in a single day, but on Gibraltar, although sinusitis was seen, it was not nearly so common. When operation was necessary in chronic maxillary sinusitis, he nowadays invariably carried out a Caldwell-Luc operation, and his experience was that this operation was very effective; his routine method was first to carry out lavage on three occasions, and if the condition did not clear up then a Caldwell-Luc was done.

W. I. Daggett said that in the Central Mediterranean area where he was stationed the incidence of sinusitis was extremely low. During a period of two years and three months when British troops numbered about 24,000, he operated upon only three cases; on one of those cases he carried out a Caldwell-Luc operation. All the bathing was in the sea. One very common nasal complaint which he found in the garrison of Malta, where the circumstances were very trying, was functional nasal catarrh. A great number of the cases showed a mild anxiety state, and amongst such patients it was extremely

common to get patients who came along complaining that they were being "poisoned" by the catarrh they were swallowing.

C. A. Hutchinson said that he was interested in the apparent association of a state of high relative humidity with the inverse occurrence of chronic sinusitis. He had spent two years in West Africa where there was a very high temperature and an extremely high relative humidity, but chronic sinusitis in particular—and any form of sinusitis for that matter—was practically non-existent there, and the main ear, nose and throat work consisted of various forms of nasal and aural myiasis. He had also spent four years in Central India, where there was an extremely high temperature—for about six weeks of the year the shade temperature was 116° —and here again there was a fairly high relative humidity, except in the "hot weather", when it was very dusty. In that part of the world there was a certain amount of sinusitis, particularly of the chronic type, but its incidence was not unduly high. In Northern India and on the Frontier, where he had spent more than four years, one had again extremely fierce heat but absolute dryness throughout a long "hot weather", with a great prevalence of a dusty wind comparable to the "khamisin" mentioned by previous speakers. There he had found a very high incidence of chronic sinusitis, though during a brief "cold weather" a large number of acute antra were seen. The site of chronic sinusitis found in Northern India was mainly frontal and ethmoidal, necessitating operative intervention—and cases had done well. It seemed to him that there must be some inverse relation therefore between the degree of relative humidity and the amount of chronic sinus infection to be found in a particular area.

J. Angell James said that his experience in the Middle East extended only over five months, as the greater part of his time overseas was spent in Italy and North Africa. In Cairo, his experience was very much the same as that brought forward by Mr. Lumsden, except in so far as the seasonal incidence of acute sinusitis was concerned. He arrived there at the beginning of August, which was regarded as the peak period for sinus trouble. A moderate number of cases were seen during that month, and the numbers fell during September and October, but in November they increased again and during December there was an epidemic, with many more cases than were seen in the summer.

With regard to the treatment of these cases they were fortunate in having ample supplies of penicillin. Many of the cases cleared up with hospitalization and treatment with penicillin and sulphonamides, and ultra-short wave therapy. The symptoms disappeared within a week, and the cases were seen again at the end of a fortnight, and at the end of three weeks skiagrams were taken. Not more than 10% failed to respond. (Local chemotherapy was used for those that failed to clear up completely with systemic treatment.) He himself had suffered from a severe attack, but the active phase lasted only four days, and on the sixth he started work again. In two weeks his sinus skiagrams were again clear.

It was considered that cases showing gross ethmoiditis were not suitable for operation in hot and dry climates, so that with few exceptions only antral operations were performed, and there he always used the Caldwell-Luc method, because his experience was that the cases which did not respond to local chemotherapy invariably had polypi or gross thickening of the mucosa in the antrum. Mr. McKenzie had mentioned the relatively small number of cases of allergic rhinitis seen in Egypt; at home he thought that 10% of all out-patients had some allergic signs, but in Egypt not more than 2% showed them.

J. A. Kilpatrick said that his experiences were very similar to those of Mr. Lumsden. The water in Egypt was definitely over-chlorinated, resulting in his own case in a stinging of the eyes which went on to conjunctivitis, wholly due, in his opinion, to the amount of chlorine in the water. He felt that probably the additional chlorine had an effect on the nasal mucosa, giving any organisms present an easier task. He had gone on to Malta from Egypt, and there he had an acute frontal sinusitis and recovered only after five weeks.

B. S. Carter said that he had been very much impressed in the Middle East, and even more so in Madagascar, with the high incidence of sinusitis in the South African troops. He was even more surprised to find how many of these South African troops had previously had radical surgery. The Caldwell-Luc operation seemed to have been carried out in South Africa on a much more extensive scale than in this country. As a rule, these cases seemed to do badly, but how much was due to a functional element he did

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					Operation
Results of treatment of antral infection					
<i>Acute and subacute</i>					
	Improvement :	Rest and inhalation	20	No improvement :	Lavage
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		Operation	10		
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Section of Radiology

President—W. M. LEVITT, M.D., F.R.C.P.

[January 18, 1946]

Tomography in the Diagnosis of Lung Carcinoma

By J. BLAIR HARTLEY, M.D., F.F.R. D.M.R.E.

THE diagnosis of chest lesions, and particularly as between primary carcinoma of the lung, primary mediastinal tumour, and mediastinal metastasis, frequently proves exceedingly difficult, and is sometimes impossible. Yet, as the possibilities of cure or alleviation by surgery or radiotherapy increase, early diagnosis becomes the more imperative. Both of these increasingly effective weapons demand accuracy in the final differential diagnosis; the former to decide the question of operability and the latter to enable radiation dosage to be planned, and the case marked down for full treatment or palliative dosage, or dismissed as unsuitable for either type of treatment.

From the radiotherapeutic viewpoint it is necessary not only to make the diagnosis but to prove it; not only to establish that the lesion is present but to demonstrate its depth and extent. None of the older methods enabled all these points to be established, and even a combination of radiography, bronchography and bronchoscopy could fail in one particular or more.

The diversity of appearances presented in carcinoma of lung or in mediastinal tumour makes radiological diagnosis from routine films difficult, and intensive study of proved cases and careful attention even by means of an efficient follow-up system fail to supply the student with any trustworthy memory-pictures with which to build up a mind-picture of either. This is due in part to the simulation of the one condition by the other, in part to the failure of bronchoscopy to demonstrate or prove by biopsy the existence of carcinomas in the less accessible bronchi or of those not within the bronchial lumen; and in part to the fact that so few cases actually die in hospital and thus come to post-mortem. Furthermore, these methods of investigation either fail in, or are unsuited to the re-examination of cases which have been subjected to radiation therapy.

The following table reveals that from 1940 to 1944 the number of cases of primary carcinoma of the lung referred for treatment each year had multiplied 3.3 times, whilst the number of cases with malignant disease of the mediastinum had multiplied 2.5 times. Note also that the cases listed as "not treated, too advanced", in the carcinoma of lung group, increased strikingly during this period. The total number of cases occurring in

not know. In Madagascar there seemed a tendency to a great deal of functional complaint. People came along saying that their sinuses were unsatisfactory and on examination one felt that further surgery was contra-indicated; they did not seem to improve on ordinary conservative measures, and a number had to be invalidated back to South Africa. His own experience of the climate of South Africa was just a passing one, but he supposed that it was rather drier than in England, and it did appear to him that the South Africans were more prone to the symptoms of chronic sinusitis.

T. B. Jobson said that he recalled a large number of such cases being in the hospital at Cairo in the war of 1914-18, and he remembered receiving a chit from headquarters asking him "if his operations were really necessary". It appeared that a slight deviation of the septum which in this country caused no particular trouble changed its character in Egypt, and became the cause of a good deal of complaint. At all events he had a large number of men who had not a very marked deviation who in Egypt made the complaint of inability to breathe properly.

The President said that one interesting statement was that sinus infection was more common in areas where living quarters were close, suggesting that sinus trouble was infectious. Possibly it was, but one wondered what happened in slum quarters where living conditions were worse than in crowded camps.

J. Angell James, in reply to a question by the President, said that the cases he had mentioned were diagnosed on clinical and radiological signs and followed up radiologically afterwards. (Swabs were taken before embarking on penicillin treatment.) Proof puncture was not performed except in cases that failed to respond, because he did not consider it advisable to puncture sinuses during the early stages of acute sinusitis.

R. B. Lumsden agreed that little or no trouble was experienced from sea bathing and that chlorination of fresh water swimming pools might be a precipitating cause of sinus infection. In a warm climate, people indulge in swimming while suffering from colds; this might aggravate an infection already present in the nose. He himself suffered from hay fever at home, but except for one week, while living with orange groves around him, he never suffered from hay fever in the Middle East. The operation figures he had given were the collective figures of all the surgeons in the Command.

J. P. Stewart, in reply to a question, said that it was quite impossible to make any comparison between the intra- and extra-nasal operations on the antrum in this series because only one intranasal drainage was carried out as against 31 extranasal operations. He was in complete agreement with Dr. Scott Stevenson's remarks as to the positive value of the Caldwell-Luc operation.

William McKenzie said that he had not found the number of septum operations to be higher in Cairo than in England, and he had never performed a submucous resection in candidates for air crew, in the absence of symptoms on the ground.

Section of Radiology

President—W. M. LEVITT, M.D., F.R.C.P.

[January 18, 1946]

Tomography in the Diagnosis of Lung Carcinoma

By J. BLAIR HARTLEY, M.D., F.F.R. D.M.R.E.

THE diagnosis of chest lesions, and particularly as between primary carcinoma of the lung, primary mediastinal tumour, and mediastinal metastasis, frequently proves exceedingly difficult, and is sometimes impossible. Yet, as the possibilities of cure or alleviation by surgery or radiotherapy increase, early diagnosis becomes the more imperative. Both of these increasingly effective weapons demand accuracy in the final differential diagnosis; the former to decide the question of operability and the latter to enable radiation dosage to be planned, and the case marked down for full treatment or palliative dosage, or dismissed as unsuitable for either type of treatment.

From the radiotherapeutic viewpoint it is necessary not only to make the diagnosis but to prove it; not only to establish that the lesion is present but to demonstrate its depth and extent. None of the older methods enabled all these points to be established, and even a combination of radiography, bronchography and bronchoscopy could fail in one particular or more.

The diversity of appearances presented in carcinoma of lung or in mediastinal tumour makes radiological diagnosis from routine films difficult, and intensive study of proved cases and careful attention even by means of an efficient follow-up system fail to supply the student with any trustworthy memory-pictures with which to build up a mind-picture of either. This is due in part to the simulation of the one condition by the other, in part to the failure of bronchoscopy to demonstrate or prove by biopsy the existence of carcinomas in the less accessible bronchi or of those not within the bronchial lumen; and in part to the fact that so few cases actually die in hospital and thus come to post-mortem. Furthermore, these methods of investigation either fail in, or are unsuited to the re-examination of cases which have been subjected to radiation therapy.

The following table reveals that from 1940 to 1944 the number of cases of primary carcinoma of the lung referred for treatment each year had multiplied 3.3 times, whilst the number of cases with malignant disease of the mediastinum had multiplied 2.5 times. Note also that the cases listed as "not treated, too advanced", in the carcinoma of lung group, increased strikingly during this period. The total number of cases occurring in

the area served by this hospital (Christie Hospital and Holt Radium Institute, Manchester) must be still greater, for this table includes few early cases, since these are very largely filtered out by the thoracic surgeon (Mr. Graham Bryce).

TABLE I.—ANALYSIS OF CASES OF MALIGNANT DISEASE OF THE LUNG AND MEDIASTINUM REFERRED TO THE HOLT RADIUM INSTITUTE, 1940-1944.

Year	Total No. referred	Malignant disease of lung			Total No. referred	Malignant disease of mediastinum		
		No. treated by radio- therapy	No. not treated			No. treated by radio- therapy	No. not treated	
			Too advanced	Patient's re- fusal, &c.			Too advanced	Patient's re- fusal, &c.
1940	33	21	0	3	10	0	1	—
1941	67	55	8	4	11	10	1	—
1942	80	51	21	8	15	12	2	1
1943	118	66	48	4	20	14	4	2
1944	110	56	54	—	25	18	6	1
	Total 408	249	140	19	81	63	14	4

My predecessor, the late E. W. Twining, was one of the first of British radiologists to recognize the value of tomography in chest examinations, and it was his original "simple attachment to the Potter-Bucky couch" which I have used throughout these investigations. (Photographs of Twining's apparatus were shown on the screen.) It continues to function satisfactorily and has required no modification beyond re-calibration, when it was found to be "recording" a stratum or plane 1.0 cm. above that actually shown on the tomograms; probably an error in the original calibration.

Of its limitations and disadvantages I am aware—the table-top is a curved one, the tube-travel is inevitably in the long axis of the chest, and the tube does not tilt but simply passes over the chest as the film passes in the reverse direction under it—but the point to be emphasized is that this apparatus has provided tomograms, which, examined critically over a number of years, have proved of great value both to diagnostician and to radiotherapist.

My claims in respect of the values of this method of examination, being based on the analysis of information obtained by the use of a primitive tomographic unit, are probably an understatement of values rather than an overstatement.

Technique.—This has been limited by the fact that the table-top is curved. There is no doubt that the flat-topped table is essential for radiology.

Focus-table distance was 36 in. Table-top to film distance was 13¼ in. Length of tube shift 12 in. to 15 in. Film shift varied between 2 in. and 3¾ in. The patient was usually supine: thus the tube-shift was traversing the long axis of the patient.

Exposure: constant 100 mA. for average of two seconds. No cone was used. In place, a lead diaphragm was inserted, with an aperture in its centre calculated and cut by the Physics Department, sufficient to enable the emergent beam to cover whatever size of film was to be used. Thus, three filters were in use, for 15 in. by 12 in., 12 in. by 10 in., and 10 in. by 8 in. films respectively.

In depicting the bronchi, tomograms were obtained at planes 1 cm. apart, the usual levels being those at 9, 10, 11 and 12 cm. (or 10, 11, 12 and 13 cm.) from the table top. The extreme levels used were at 8 cm. and 14 cm. respectively.

Each tomogram was identified by the use of a lead number indicating the height-above-table-top of the plane or section.

Thus, particularly in dealing with small or localized lesions likely to be irradiated, the depth of the centre of the lesion was rapidly established, whilst the limits of the lesion were delineated, although with a lesser degree of accuracy.

The demand for tomography arose in the Holt Radium Institute chiefly for the following reasons:

First because the established diagnostic method of bronchography using lipiodol was contra-indicated, the therapists objecting on the grounds that treatment was already sufficiently difficult without introducing the factor of an unknown quantity of iodine within the lung.

Secondly there was the necessity to localize the treatable lesions in depth and if possible in extent.

Thirdly it was recognized that bronchoscopy was of limited value in that not all carcinomas (obstructive or otherwise) lie in situations visible or reachable by the bronchoscope. Thus bronchoscopy was helpful if it produced a positive finding and/or a positive biopsy result; but it was valueless if it afforded only a negative report and/or a negative biopsy, or an indeterminate one.

Lastly, wartime conditions made imperative exact and rapid reviews of individual case problems.

Value of tomography.—Tomography though not, in itself, a diagnostic method, is, nevertheless, of great diagnostic value. It has been shown to be exceedingly accurate in the demonstration of carcinoma within or deforming the walls of the bronchi. Lesions of upper lobe bronchi or their branches, for example, are depicted and diagnosed with ease and reliability. And so the values of this method are assessed as follows:

(1) In confirming the existence of obstruction of a bronchus already diagnosed and in demonstrating its probable site of origin; or alternatively in rejecting such a diagnosis, where the bronchi were shown to be normal.

(2) In demonstrating the size and/or depth of a carcinoma already diagnosed, and in revealing the true nature of lesions undiagnosed or inaccurately diagnosed. For radiotherapy purposes localization and indication of extent of lesion, and sometimes of the "treatability" (e.g. by proving mediastinal metastasis not otherwise demonstrable) were of great value.

In this respect the criticism has been raised that an A.P. view taken on the Potter-Bucky table, and "over-penetrated" is quicker to obtain and just as reliable. It is true that such a film may show the lesion, but even if it does (and it frequently fails), it does not localize the lesion in depth or extent.

(3) In demonstrating whether one is dealing with a carcinoma of obstructing or ulcerating type, or whether the lesion is extensive and of the peribronchial infiltrating variety.

(4) In revealing detail, which may enable the radiologist to assess not only whether the case is one of carcinoma of lung, or of mediastinal tumour, but if in the latter group, to suggest the probable nature of the mediastinal invasion. In this connexion it is suggested that where the borders of the tumour can be clearly defined, or where the tumour is seen to push or compress the trachea or bronchi, the tumour is more likely to be a variety of Hodgkin's disease.

(5) Where the invasion occurs without compression or displacement of the air passages, and when its limits are extensive and ill-defined, and particularly if there are comparatively few symptoms, the probability is that one is dealing with a lesion likely to prove very sensitive to irradiation (probably lympho-sarcoma).

(6) Tomography can be exceedingly useful as an aid in determining whether any changes revealed in the chest picture during the follow-up period are due to recurrence of the treated lesion, or whether they are due to mechanical deformities resulting from fibrosis, which, in turn, may result from treatment.

(7) Lastly, it is anticipated that, particularly in the group of obstructing or ulcerating lesions of the bronchus, serial tomography will be of assistance in determining more precisely, both the immediate and the late effects of radiation therapy.

Since the lesions can be seen more clearly by this method, it should be possible, when a sufficient number of proved cases have been reviewed, to decide not only how much the tumour has receded, but possibly also the site at which any recurrence has taken place.

Limitations of tomography.—Tomography does not necessarily indicate the exact nature of the lesion, and even in the case of obstructive lesions, the diagnosis may be indeterminate, as between a simple tumour, carcinoma, or an inflammatory process.

Secondly, although it may, on occasion, be of assistance in deciding how much of the lesion depicted in the routine radiograph is due to malignancy, and how much to infection, the method is frequently unreliable in making this distinction.

Thirdly, very early or very small lesions, whether in lungs, trachea, or main bronchi, are not easy to demonstrate, and may readily be missed. It is in the detection of these small foci that detailed improvements in tomography technique are required.

Lastly, interpretation of tomograms is probably most difficult and least reliable in the assessment of tumours arising in the right main bronchus, and particularly so if bronchiectasis be present in the lower lobe.

CONCLUSIONS

Tomography is not yet used sufficiently widely in the study of the bronchial tree, its value being yet inadequately realized in this country.

The method cannot replace routine radiography; indeed, it can only be really satisfactorily carried out after study of and with measurements obtained from both the P.A. and the lateral view.

Tomography is complementary to bronchoscopic examination, but it is of superior value in the assessment of cases in which bronchoscopic examination has afforded either a negative report or biopsy report of negative value.

The method can, and should, now replace lipiodol bronchography in chest examinations, where the case is likely to be one of carcinoma of the bronchus, and where radiation therapy is indicated. Tomography is easier and quicker; an important advantage in a large clinic, where the case should be diagnosed, assessed, and even treatment planned, before the patient leaves, possibly to return to a far distant home.

Accuracy of diagnosis by tomography demands fine focus tubes, and at the moment a rotating anode tube is an essential feature of any respectable tomographic unit. Increased accuracy of diagnosis is probably related to the distance between the layers or strata selected. A fair degree of accuracy can be obtained by using strata at 1 cm. intervals, but in difficult cases it is probably wise to repeat the examination of the suspected area, using layers at 0.5 cm. apart.

The increasing number of patients presenting themselves with malignant lesions of lung or mediastinum, and the possibility of more effective radiation therapy, afford a wider field for tomography in radio-diagnosis.

Some Observations on Radiology of the Pancreas

By R. A. KEMP HARPER, M.B., D.R.

RADIOLOGY has come to play its important part in the recognition of pancreatic disease as clinical means of diagnosis are still in an elementary stage due to the paucity and indefinite nature of the symptoms. One cannot therefore emphasize too strongly the necessity of looking for evidence of such disease in all obscure cases with upper abdominal symptoms.

All too frequently an examination of the stomach and duodenum ceases when the duodenal cap has been inspected. We must acquire the habit of carrying out careful inspection until the upper coils of jejunum have been adequately visualized, otherwise many pancreatic lesions will remain undisclosed.

Tests of efficiency are still inconclusive in many cases of extensive pancreatic disease, as they are in tests for hepatic function.

SYMPTOMATOLOGY

Acute pancreatitis is usually an urgent surgical emergency and is seldom diagnosed pre-operatively. Pancreatic calculi and calcification are diagnosed mostly as unexpected findings in a film of the upper abdomen and confirmed by the demonstration of their close relationship to the stomach and duodenum after a barium meal study.

Chronic pancreatitis and cyst give rise in the main to vague symptoms, unless the cyst is sufficiently large to be easily palpable clinically. The symptoms are usually those of recurring indigestion of a type not periodic in relation to meals, although exceptionally it may be so. Gaseous distension and upper abdominal tenderness are common features.

Jaundice is an occasional factor in chronic pancreatitis but is a more common finding in carcinoma of the pancreas which may be suggested clinically if there is persistent deep-seated boring pain passing through to the back, a feature of carcinoma of the body or tail infiltrating posteriorly to involve the spine and nerve roots, and coeliac ganglion. There is often also a steady loss of weight as in so many malignant conditions.

Finally, chronic pancreatitis may give rise to changes in small intestinal motility and function as have been frequently reported in the last few years.

RADIOLOGICAL INVESTIGATION

Pneumoperitoneum was persistently advocated by Carelli (*see Case, J. T.*) of Buenos Ayres for some years but he has now modified his views and states that were it not for the frequency of hydatid disease in South America he would find little indication for its use.

Gastric pneumography has been frequently advocated since Engel and Lysholm (1934) introduced this method in 1933, its latest advocate being Thomas (1945) of San Francisco but although in selected cases it may be of assistance as an additional aid, there is no doubt that the routine barium meal with full examination of the duodenum as well as of the stomach, is the most satisfactory method as the mucosa of the duodenum and stomach can be studied in detail to determine the presence or absence of erosion, whilst motility and the finer details of contour cannot be seen by any other means.

The findings of opacities of doubtful nature in the upper abdomen should always be fully studied by postero-anterior and lateral films, and usually also by gastro-duodenal examination to define their relationship to these viscera.

Calcification.—Calcification in the body of the pancreas is occasionally encountered (figs. 1 and 2), and it may also be found as the result of a preceding acute pancreatitis (fig. 3). Calculi have occasionally been reported in the ducts.

The size of the pancreas can be fairly well estimated by the distance between the anterior surface of the spine and the posterior wall of the stomach after gastric visualization either by air or barium; the former is effective in enlargement of the body or tail but the latter is essential for adequate examination of the head. This distance is normally equal to that of the diameter of the body of the vertebra at the same level but in stout subjects it may be considerably greater and in such patients a definite opinion can only be expressed in marked examples.

Cyst formation.—Cystic enlargement is the most easily recognizable of the causes of pancreatic disease in virtue of the smooth-filling defects produced in the parts of the gastro-intestinal tract in close relation to the pancreas. The displacement caused by the cyst varies according to its position and the direction in which the cyst enlarges.

Whilst diagnosis may be easy, it is on occasion extremely difficult and the main conditions to be considered in differential diagnosis are mesenteric and omental cysts, renal cysts and enlargements, retroperitoneal sarcomata, hydatid cysts and hydrops of the gall-bladder, suprarenal tumours and aortic aneurysms.

Cholecystography and urography may also be necessary.

Porta and Roversi illustrate six types of cystic enlargement according to their effect on the surrounding viscera:

(1) Cyst of the head—enlarging and flattening the duodenal loop and causing pressure deformity of the antrum.

(2) Cyst of the body—frequently displacing the stomach upwards.

(3) Cyst of the tail—displacing the greater curve medially and the transverse colon downwards and laterally.

(4) Gastro-hepatic type which displaces the lesser curve downwards and often the third part of duodenum and the transverse colon also (fig. 4).

(5) Gastro-colic type displacing the stomach medially and the transverse colon distally (fig. 5).

(6) Mesocolic type displacing the stomach and transverse colon proximally.

Carcinoma of the pancreas is now being recognized with frequency, largely as a result of the greater awareness of radiologists and of more detailed study of the duodenum as a whole. The head is the commonest site but the body is also frequently affected, a lesion of the tail being much less common. Diagnosis depends on the deformity produced and presence of infiltration of stomach or duodenum. Although carcinoma of the head of the pancreas frequently causes jaundice by obstruction of the common bile duct or ampulla, it is surprising that a fair-sized carcinoma may not involve the ampulla until late in the course of the disease. When the lesion is situated in the region of the ampulla it may produce the appearance described by Frostberg (1938) as a reversed 3 but this occurs in a fairly small proportion of cases of carcinoma of the head of the pancreas and may be present in other types of pancreatic enlargement.

Widening of the duodenal loop and a pressure effect are insufficient evidence on which to diagnose carcinoma although frequently these constitute the only radiological evidence for a long time. The additional factor of erosion or invasion of the duodenal wall or stomach must be found before diagnosing malignancy (fig. 6). A further type is that which produces an annular narrowing of the descending duodenum and which may in certain cases arise from a so-called annular pancreas where the head almost surrounds the duodenum.

Occasionally, enlargement occurs high up in the head of the pancreas and produces a fairly characteristic appearance of the duodenum which is stretched out in the form of a sickle over its superior aspect. Invasion of the antrum of the stomach is also sometimes a feature of carcinoma and difficulty in differentiating from a gastric carcinoma may be considerable unless the enlargement of the head of the pancreas is marked.

The third part of the duodenum may be heavily invaded and it may be impossible to exclude a primary malignant duodenal tumour (fig. 7).

Frequently there is, in addition, abnormal duodenal function with to-and-fro movements, exaggeration of the *plicæ circulares* and retrograde peristalsis or ileus.

Films in both erect and recumbent postures are required and the supine position is generally helpful as the duodenum rings the head most closely in this position. Prone

Accuracy of diagnosis by tomography demands fine focus tubes, and at the moment a rotating anode tube is an essential feature of any respectable tomographic unit. Increased accuracy of diagnosis is probably related to the distance between the layers or strata selected. A fair degree of accuracy can be obtained by using strata at 1 cm. intervals, but in difficult cases it is probably wise to repeat the examination of the suspected area, using layers at 0.5 cm. apart.

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FIG. 9

Arrows indicate site of enlarged glands.



FIG. 10

Arrows indicate enlarged glands within the duodenal loop.

FIGS. 9 and 10.—Enlarged pre-pancreatic glands in Hodgkin's disease causing duodenal compression and antral deformity.

Potter-Bucky films are also most useful and compression films are of great value in demonstrating minor degrees of mucosal destruction.

Lesions of the body and tail require careful examination in every position also and invasion of the stomach wall posteriorly is a helpful finding, together with localized pressure deformity.

Chronic pancreatitis.—Produces enlargement of the gland without duodenal or gastric invasion but adhesions may be present (fig. 8). In general, however, it is impossible to exclude carcinoma as the enlargement may be obvious in the latter condition before duodenal involvement is found.

Jaundice is also sometimes a feature of this condition as well as in carcinoma. Radiological differentiation may thus be as difficult as on those occasions where the hardness of the gland to palpation makes even surgical differentiation impossible.

Whilst being alive to the possibility of intrinsic pancreatic disease, we must not forget that metastases are frequent in the pancreas and other conditions may produce enlargement of the pre-pancreatic glands. This may occur as a mass secondary to a carcinoma of the gastro-intestinal tract, but also in Hodgkin's disease and lymphosarcoma (figs. 9 and 10). Retroperitoneal sarcoma and many other conditions malignant and nonmalignant may also produce glandular enlargement or simulate it.

A tremendous advance in diagnosis will be made when excretory pancreatography is in general use but until a suitable excretory substance is available we must constantly endeavour to raise the standard of accuracy by our present methods, in the diagnosis and differentiation of pancreatic disease. Nor is it probable that examination of stomach and duodenum will even then be dispensed with, as a means of assessing the size of the gland, and its relation to and effect on surrounding viscera will still be required.

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FIG. 1

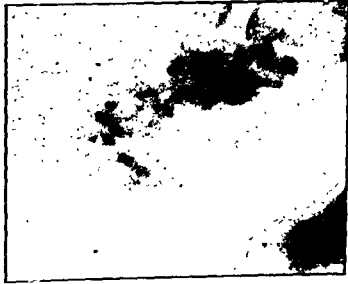


FIG. 2

FIGS. 1 and 2.—Calcification of parenchyma of pancreas.]



FIG. 3.—Calcification of head of pancreas following acute pancreatitis.



FIG. 7.—Extensive invasion of duodenum by carcinoma of pancreas.



FIG. 4.—Deformity of stomach due to gastro-hepatic type of pancreatic cyst.



FIG. 5.—Displacement and deformity of stomach from pressure by a pancreatic cyst of meso-colic type.



FIG. 6.—Carcinoma of pancreas showing early duodenal invasion.

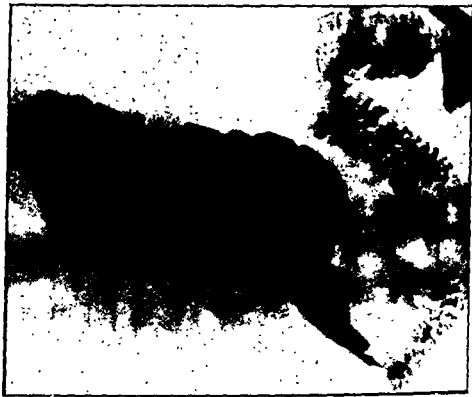


FIG. 8.—Duodenal compression between gall-bladder and pancreas enlarged by cholecystitis and pancreatitis.



FIG. 9

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Experimental Study of the Vertebral Venous System—Preliminary Report

By A. S. JOHNSTONE, M.B., Ch.B., F.R.C.S., D.M.R.E.

A CLAIM to have found a new route for the spread of metastases is of particular interest to radiologists, and, in presenting this paper, I propose first to summarize the work published by Dr. Batson of Philadelphia (1940) and then record the results of experiments made in an attempt to confirm it.

At the outset I would like to acknowledge the kindness of Dr. Batson in answering my requests for information. His ready response with lucid explanations has left me with a sense of misgiving that somewhere in my experiments a technical error has been committed; but, with the exception of the medium used for injection, the work has been carried out according to his directions.

In 1938 Batson reported a description of the vertebral venous system which he considered to be independent of and quite distinct from the caval, pulmonary and portal systems. It is comprised of complex, interlacing tributaries running along the spinal canal and ramifying in and around the vertebral bodies; it has few valves, very little permanent flow and the pressure is low. The system, in other words, acts as a reservoir of moderately large volume. It is in free communication with the iliac, lumbar, azygos and cranial veins but it is not subject to the same alterations in pressure during coughing or straining. It may thus provide an alternative path for the venous return when the intra-abdominal or intrathoracic pressure is raised.

Batson demonstrated this system in cadavera by the injection of radiopaque material into the deep dorsal vein of the penis. In his earlier attempts he injected a viscid substance—King's yellow—which filled the main caval veins, but, after using vermilion water colour, described as having the consistency of light machine oil, the vertebral system was clearly demonstrated while the caval veins remained empty. The explanation offered for this change of route was that the vertebral veins lay at a lower level than the caval veins—the cadaver lying in the supine position—and the medium of low viscosity freely entered the vertebral system. The greater the quantity injected the further the medium spread up the vertebral column until veins in the skull were filled. The injections were made under fluoroscopic control and stereoscopic radiographs showed the medium to be within the bones.

He extended his experiments to living monkeys and found that on injecting thorotrast into the deep dorsal vein of the penis the inferior vena cava was filled, but, after compressing the abdomen by a tight band, the medium passed into the vertebral system. Batson was forcibly struck by the similarity as shown in the radiographs between the distribution of the opaque venous channels in and around the sacrum, lumbar spine and ilia and the distribution of metastases from cancer of the prostate.

He then discussed the possible methods of spread in these cases. The lymphatic permeation theory of Handley (1922) was dismissed as improbable and the work of Warren on the perineural lymphatic route was scarcely considered. He agreed that metastases were blood-borne but did not favour a spread through the lungs as accepted by many pathologists, notably Willis (1934). He contended that the act of straining would disseminate malignant cells into the vertebral plexus where they would readily settle in or around the adjacent bones and might even pass up into the skull.

To test his hypothesis he injected small mammary veins and found that the opaque medium passed readily into the vertebral system, via intercostal and scapular veins, and thence spread up and down the spine finding its way to the skull, the pelvis and femora. The medium, in addition, entered the upper ends of the humeri and clavicles and the entire distribution corresponded to the spread of breast cancer.

Batson contended further that the free communication of the bronchial veins with this plexus explained the intracranial spread of metastases from bronchial carcinomata and lung abscesses. In a similar way he explained the source of air embolism following pneumothorax.

In our efforts to confirm Batson's findings we have been forced to use different media owing to the scarcity of vermilion water colour, and the bodies used have not previously

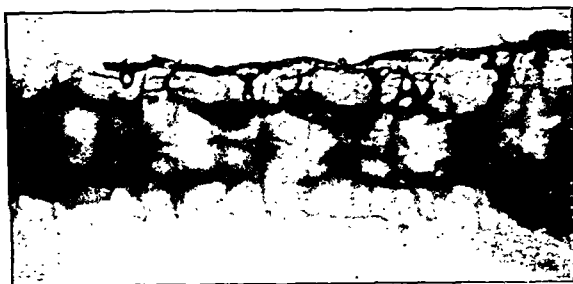


FIG. 1.—Vertebral veins filling after ligation of inferior vena cava. Medium used—crude vermilion.



FIG. 2.—Injection of vermilion without ligation. .
Most of the medium lies in the caval system.



FIG. 3.—Medium in vertebral veins as well as caval veins twelve hours after injection.

been preserved for dissection, but have been injected at varying intervals within twenty-four hours of death.

In the first experiments uroselectan and 20% sodium bromide were used and the caval veins were quickly filled. There was very little evidence of opaque medium in the para-vertebral veins so that in subsequent experiments the inferior vena cava, femoral and external iliac veins were ligated. This produced an improved filling of the sacral, ilio-lumbar and ascending lumbar veins, together with many of their small tributaries (fig. 1).

Another series of observations was made using a suspension of crude vermilion, sufficiently dilute to enter minute vessels in the kidney, so that it appeared to be an adequate substitute for vermilion water colour (fig. 2). No attempt was made to estimate the specific gravity of the medium as the vermilion was in suspension.

In some cases the bodies were injected soon after death and radiographs were taken immediately after injection and repeated some twelve hours later. Comparison of these radiographs showed less medium in the caval system and more around the vertebrae in the later films, which suggested that the forces of gravity may have been partly responsible. It was these films which most closely resembled those of Batson (fig. 3).

As a variation some lipiodol was injected into the corpora cavernosa of the penis, and this was followed by xylol to lower the viscosity. Small globules of lipiodol were washed into the venous system and several overlay the vertebral bodies, but it was not possible to localize them within the vertebral system.

One case, in which a moderate filling of the veins around the vertebrae had been obtained, was radiographed after the post-mortem examination. Very little medium remained although the paravertebral veins had not been disturbed.

In all experiments there seemed to be overwhelming evidence that the main return took place through the caval tributaries. On no occasion did the medium reach the skull, the highest point being the entry into the superior hemi-azygos vein after retrograde filling from the azygos vein. The volume of the system seemed to be relatively small. Several attempts were made to demonstrate the communications between the breast and the vertebral system without success. This may have been due to technical faults as the only veins which were sufficiently large to inject led directly to the axillary and subclavicular veins.

DISCUSSION AND SUMMARY

The experiments show that the principal venous drainage from the prostatic plexus flows into the caval system, irrespective of the viscosity of the medium used. Free communication exists with the paravertebral veins and it was felt that the forces of gravity played some part in the experimental filling of these veins. Ligation of the main caval veins did not produce any outstanding increase in the quantity of medium entering the vertebral veins.

It would appear that Batson has tried to establish the existence of a route of metastatic spread principally on the fact that the radiographs of injected pelvic and vertebral veins bear a resemblance to the radiographs of carcinomatous deposits in these bones. If his conclusions are correct it is difficult to explain the relative absence of metastases in the transverse and spinous processes if there is such free communication between the veins.

One has only to see the massive involvement of para-aortic lymph glands in advanced cases of malignant prostate to realize that, although the bone-marrow may have no lymphatics, the perineural lymphatics provide adequate channels for the cells to reach the periosteum and cortical bone, and the work of Warren *et al.* (1936) cannot be so lightly dismissed.

It is also reasonable to conjecture that if the pelvic lymphatics could be injected, the resulting radiograph would produce an appearance corresponding to the distribution of secondary metastases.

In conclusion it is felt that, although some cells may be disseminated along the vertebral venous plexus, there is no definite proof that these vessels provide the main route for the spread of metastases in carcinoma of the prostate, breast and bronchus.

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Section of Proctology

President—ERIC A. CROOK, M.Ch.

[March 13, 1946]

DISCUSSION ON THE USE OF MEDICAMENTS IN DISEASES OF THE COLON AND RECTUM

Dr. F. Murgatroyd: I shall discuss only a few aspects bearing on the treatment of amœbic infection of the bowel, as recent reports increasingly suggest the treatment of this condition to be unsatisfactory.

The drugs commonly used fall into three groups: (1) Ipecacuanha derivatives, of which emetine hydrochloride and emetine bismuth iodide are the most renowned, (2) substituted phenyl arsonates, such as carbarsone and stovarsol, and (3) iodoxyquinoline compounds, of which the chief are chiniofon and diodoquin.

Until recently emetine hydrochloride and emetine bismuth iodide were much less used in the United States of America than in Great Britain, while in the latter country diodoquin was virtually unknown. British practice favours treatment by combinations of the various classes of drugs, a common standard course consisting of emetine bismuth iodide grains 2 or 3 by mouth together with retention enemata of 2½% chiniofon daily for ten days, followed by carbarsone 0.25 grammes by mouth twice daily for a further ten days; sometimes this course is immediately preceded by emetine hydrochloride 1 grain by parenteral injection for a few days. The degree of success obtained by such treatment has been assessed variously as lying between 75 and 95%.

In any endeavour to understand the reason for the failures it is necessary to consider the parasite, the patient and the procedure.

Suggestions have been made that amœbæ may vary in their resistance to the drugs employed, and that inadequate treatment may lead to the development of increased resistance with ultimate failure of the parasite to be influenced by the drugs. There appears little sound experimental evidence to support such a hypothesis in the case of the arsenical and quinoline drugs in amœbiasis, and there are good reasons for doubting the validity of the experiments on which the claims for emetine-resistance rest. In short there seems little justification at present for attributing therapeutic failure in the treatment of amœbiasis to drug-resistance of the amœbæ.

In overt dysentery there are tissue lesions associated with invasion by the amœbæ, and it is widely believed, especially by American workers, that all patients passing *E. histolytica* in their stools, even the asymptomatic carriers, have lesions in the bowel, although these lesions may be only microscopic. However, it is possible that a proportion of the amœbæ may live as commensals, feeding on organic residues or bacteria, in the lumen or on the wall of the gut without actually invading the tissues:

Another series of observations was made using a suspension of crude vermilion, sufficiently dilute to enter minute vessels in the kidney, so that it appeared to be an adequate substitute for vermilion water colour (fig. '2). No attempt was made to estimate the specific gravity of the medium as the vermilion was in suspension.

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Lt.-Col. W. H. Hargreaves: At the Queen Alexandra Military Hospital at Shenley during the past two years, 699 patients with amœbiasis in various stages have passed through our hands.

In 1944, about one-fifth of our patients with chronic amœbic dysentery were bed-ridden with foul diarrhœa, their stools containing blood, mucus, and amœbæ. They complained of almost persistent colicky pain, and their colons were palpable and tender. Sigmoidoscopy as a rule showed extensive ulceration, the mucosa between the ulcers being swollen and injected.

These patients presented a desperate problem. Some had been under treatment for as long as 2 years, dating from the fall of Burma in 1942, when chaos reigned; it was often several weeks before they got back to India, where hospitals were overflowing and drugs scarce. By the time they reached us they had been given repeated courses of anti-amœbic drugs, often at home as well as abroad, including emetine injections sometimes running into three figures, and they had been labelled emetine-resistant. Many of them had also been given courses of sulphaguanidine or succinylsulphathiazole (sulphasuxidine). In May 1944 one of these patients died. Acting on the assumption that secondary bacterial infection was preventing a response to anti-amœbic drugs, we then tried penicillin at the suggestion of General Biggam as a last resort for an apparently moribund patient. He responded dramatically, and although the amœbic infection persisted, his symptoms subsided and on sigmoidoscopy the ulceration was seen to heal. After two courses of penicillin, standard anti-amœbic treatment was given; when finally reviewed four months later, he was still well.

The outlook of these distressing cases was changed considerably as the result of this experiment. Penicillin has not been found to have any significant effect on *Entamoeba histolytica*, but we have found repeatedly that it renders severe refractory cases of chronic amœbic dysentery more amenable to drugs with a specific action on the amœbæ. The symptomatic relief is very striking. Patients transferred to us on the dangerously ill list needing morphia to relieve their pain have become free from colic after two or three days on penicillin and have begun to pass formed stools. Repeatedly on sigmoidoscopy during the course of penicillin treatment we have seen improvement, the swelling and injection of the mucosa subsiding so that ulcers become more superficial in appearance and begin to epithelialize.

We now give a course of penicillin which lasts just over eight days, totalling 2 million units, in three-hourly doses of 30,000 units intramuscularly. To combat some of the organisms which are not sensitive to penicillin we also give sulphasuxidine at the same time by mouth—20 grammes daily. Occasionally it has been necessary to repeat the course—for instance, in one case where numerous small abscesses could be seen bursting through the mucosa when the sigmoidoscope was introduced.

The anti-amœbic treatment which we give to chronic cases now usually consists of a 12-day course of emetine bismuth iodide—3 grains of the loose powder in 1 gramme gelatin capsules at night—combined with daily retention enemata of chiniofon, followed by a course of diodoquin—three tablets thrice daily by mouth for twenty days. Tests of cure are carried out one month after the end of this treatment. Three of the first 50 cases relapsed after this period. One of these had refused to have any more EBI after his penicillin course. We had no comparable series of patients treated with anti-amœbic drugs only, as the cases described were very severe and had previously been given repeated courses of routine treatment without success.

This success with penicillin in chronic amœbic dysentery naturally led us on to try it in chronic ulcerative colitis. Claims for any treatment in this disease must be made very timorously owing to its notorious tendency to remit spontaneously. As luck would have it, however, our first patient appeared to respond well. This was a woman aged 30 who had been ill for eighteen months, during which she had been treated with medicated enemata and sulphaguanidine. She was critically ill and sigmoidoscopy showed severe ulceration. Two weeks after the end of a course of penicillin and sulphasuxidine, her symptoms had subsided and sigmoidoscopy was normal. This was in October 1944, and since then she has remained well apart from periodic constipation, and in fact she has married. When I saw her last month, sixteen months after the treatment, she was free from symptoms and her bowel was normal on sigmoidoscopy.

Our second patient had regional colitis and had been treated previously with sulphaguanidine and sulphasuxidine without success. He was symptom-free and normal on sigmoidoscopy following two courses of penicillin and sulphasuxidine separated by an

such parasites might presumably be little influenced by amœbicidal drugs present in the blood and tissues, in which case successful therapy might depend upon having an adequate concentration of drug in the contents of the bowel. Unfortunately to this question of precise pathology a certain answer cannot be given.

There are also vexatious uncertainties regarding the exact state and distribution of the drugs themselves in the body. For example, emetine, which *in vitro* has such a potent direct action upon *E. histolytica*, fails when injected parenterally, to cure intestinal infections with this parasite in cats. In these animals the drug appears largely to be eliminated in the urine, and it may be that this mechanism prevents the tissue-concentration of the drug from rising to, or being maintained sufficiently long at, an amœbicidal level. Alternatively, these animals may metabolize or render impotent the drug in some manner different from that obtaining in man. Even in man, however, there is abundant evidence to show that daily injections of emetine hydrochloride 1 grain fail to cure a large proportion of intestinal infections, some placing the relapse rate as high as 90%, and with chronic carriers the results are particularly poor. It may be that comparatively small differences in the metabolism or elimination of the drug between individual patients may become manifest clinically by the gross difference between cure and relapse. Save in a small percentage of patients, emetine hydrochloride 1 grain daily appears either insufficient to maintain in the tissues an amœbicidal milieu for a sufficient length of time to eradicate the infection or it fails to destroy the parasites in the lumen of the gut, and so relapse occurs. Yet this method of treatment appears to be considered adequate, especially in India.

On the other hand, Dobell found almost thirty years ago that emetine bismuth iodide 3 grains daily by mouth for 12 days cured about 90% of carriers of *E. histolytica*. From this it would appear that a comparable amount of emetine given by mouth may, possibly owing to slower absorption, maintain an amœbicidal concentration of drug in the tissues or gut for a more prolonged period, and so sterilize the infection. It may not be without significance in this connexion to note that when emetine is given by mouth only on alternate days, as auremetine in the course employed at Liverpool for many years, a relapse rate as high as 90% has recently been recorded for chronic infections so treated.

The necessity for giving emetine bismuth iodide in a suitable form so that it becomes liberated and dispersed, and possibly absorbed, seems generally agreed, even if often neglected in actual practice. It may also be necessary to maintain the dosage at 3 grains daily, and the suggestion of recent years that 2 grains is sufficient may not be without danger. The addition of emetine hydrochloride parenterally in "loading" doses at the beginning of treatment with emetine bismuth iodide seems reasonable, but I am not convinced that the addition of chiniofon, carbarsone or similar drugs materially improves the ultimate result, although, in the present state of our ignorance and since there is no evidence of any "interference phenomenon" when such drugs are used together, it would seem justifiable to retain their association.

Some years ago attention was drawn to the possible part played by concomitant bacteria in the survival and invasiveness of the amœba; and more recently Colonel Hargreaves, being impressed by the secondary infection of the bowel of a fatal case, tried the effect of associating penicillin and succinylsulphathiazole with the specifically amœbicidal drugs. He observed that œdema and hyperemia of the mucous membrane subsided and that the ulcers became more superficial when treated with the penicillin and the sulphonamide compound; and he stated that "there seems little doubt that in this way the amœbæ are rendered more easy of access to emetine." Whether this be true or not, it would appear that his view is that emetine remains the ultimate amœbicidal agent, and it is difficult therefore to believe that penicillin and sulphonamide can make much difference statistically to the total results of treating amœbiasis, since in general the cases refractory to treatment are not necessarily those with gross lesions. In fact most authors stress the greater difficulty of sterilizing the chronic cyst carriers, in whom lesions if present at all are often minimal. It would therefore be of great interest to know whether the combined treatment does in fact confer any benefit in the treatment of the less acute and less severe cases. While there seems no doubt of its value in gravely advanced and secondarily infected cases, the primary aim should be to eradicate the infection before the patient reaches such a state. To this end the great practical need is a wider appreciation and application of what is already known about the treatment of amœbiasis, while fundamentally further insight is desirable into the mechanism of action in man of those drugs which, properly used, still justify the promise they revealed more than a quarter of a century ago.

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tive amœbæ in the stools, and is given intramuscularly, 1 grain daily for four to eight days. When symptomless amœbic ulceration or cysts are chance findings no intramuscular emetine is required. EBI and chiniofon are then started at once.

With emetine injections a fall in blood-pressure occurred only if given for longer than eight days. Blood-pressure records were, therefore, regarded as unimportant with standard dosage. All our subjects, however, were European or American troops; reactions may admittedly be commoner in Indians whose physique is slighter.

The injections are followed without a break by the course of EBI, twelve consecutive daily doses of 3 grains by mouth, together with retention enemata of chiniofon. EBI is normally dispensed in gelatin or sugar-coated capsules both of which render disintegration and absorption uncertain. We gave it direct as powders either in a spoonful of jam or on the back of the tongue with a drink. EBI is customarily administered at night with a barbiturate sedative to allay the nauseating effect, but we found it was well tolerated and toxic effects need not be anticipated. The stools should always be inspected as a control of assimilation; they are dark from the bismuth in the compound.

Chiniofon enemata, consisting of 7 oz. of 2½% solution daily for these twelve days, were given simultaneously with EBI. (Synonyms: yatren, quinoxyl, quinosulphan.) To help to retain each enema for at least six hours the foot of the bed is raised on 8 in. blocks. The patient should lie in turn, for half an hour each on his left side, back and right side. This drill keeps him recumbent but has no other particular value, for we have shown by X-rays that enemata reach the cæcum from the supine position. Patients will often tolerate with benefit a gradual increase both in volume and strength of the enemata. Towards the end of the EBI course some diarrhœa is common and upsets retention unless an alkaline bowel washout is given before. In a busy ward the sterilization of apparatus must be supervised to prevent cross infection of bacillary exudate.

Finally, for a further twelve days, carbarsone (or stovarsol) was given, 4-grain tablets twice daily, to eradicate cysts, and the patient was then allowed up.

We had a small experience of Kurchi bismuth iodide at a time when EBI was scarce but were not convinced that it replaced EBI as an active amœbicide.

Emetine resistance.—One has learnt that interruption of treatment is a cogent cause of chronicity and relapse. Its relative incidence is high, for example, among doctors, because we are sometimes too impatient to undergo the prescribed full course and are inclined to modify it to our convenience. In one's earlier experience, when treatment was not standardized and soldiers were denied the proper drugs through short supply, relapses were common and many apparently intractable cases were invalidated home. We now realize that few of these so-called emetine-fast cases had a completed course of treatment controlled in hospital. Latterly it became rare, except for operational reasons, to evacuate any patient with chronic amœbiasis. Emetine resistance clearly is more apparent than real. There are perhaps exceptional cases which do not at first respond to standard treatment, yet even these will generally react to a second course repeated after an interval, when penicillin and sulphasuxidine may be needed to clear secondary colonic infection.,

CONCLUSIONS

The continuous sequence of treatment is all-important. Hypodermic emetine deals only with initial symptoms; by itself it does not cure. EBI (by mouth) and chiniofon (enemata) are possibly the keystones of treatment. Carbarsone should clear residual cysts. The twelve-day periods in therapy are arbitrary; they may be prolonged but never reduced. Bed-rest is essential for the first two to three weeks but diet restriction and purges are not. Convalescence for three weeks is desirable, followed by readmission to hospital for six daily stool tests of cure and final sigmoidoscopy.

Mr. T. Howard Somervell: South Indian experiences in colonic disease.—*Amœbic dysentery:* Most of our work in the medical wards seems to be clearing up the failures of other doctors by giving continuous courses of emetine to patients who have already had scores of injections, but never more than five or six at one time.

Amœbæ often disappear from the stools, so do blood and the characteristic degenerated leucocytes, after six emetine injections. The patient feels that he has "had enough," and the doctor, always willing to please, lets him off for a few days before giving more emetine. The patient recovers his composure, so do the amœbæ. They have had a kind

interval of two weeks during which daily retention enemata of sulphasuxidine were given. He relapsed after seven months, but has responded again to another course of treatment.

We have treated 7 other patients with ulcerative colitis and proctitis. All showed a satisfactory response, but 2 had persistent granularity in the lower part of the rectum—one after four courses of treatment. Only one patient had a ribbon-like colon radiologically, and there was no change in this appearance after treatment, although ulceration had healed. These patients were definitely improved, but one cannot claim that they were cured.

Our clinical experiences are open to the criticism that they did not always have strict bacteriological control. Occasionally we have been able to isolate penicillin-sensitive streptococci and staphylococci from the dysenteric cases, and in 2 cases of ulcerative colitis penicillin-sensitive staphylococci have been found.

My conclusion is that penicillin is well worth a more extensive trial in chronic ulcerative colitis.

I mentioned our first case of ulcerative colitis in November 1944 at a meeting of the Royal Society of Tropical Medicine and Hygiene. After this meeting, Sir Alexander Fleming was asked to give penicillin to another patient who was being despaired of after seven months' illness. He did so, after isolating penicillin-sensitive staphylococci. The patient recovered, and has remained well now for over a year.

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Diagnosis.—From a study of tropical disease in the tropics one learns that its behaviour may differ much from the classical teaching. Although chronic amœbiasis was an important cause of insidious ill-health in South East Asia Command, cases were rarely labelled "chronic amœbic dysentery" as a first diagnosis because the symptoms are generally more negative than positive. Diagnosis from the history alone is difficult since dysentery *per se* is not a regular feature of chronic amœbiasis and, even at the onset, can be mild and pass unnoticed. Indeed, in an endemic area, while an individual is becoming acclimatized, short bouts of diarrhoea are usual.

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Not uncommonly a latent chronic amœbic infection was brought to light by the activation of an intercurrent acute illness, for example malaria or bacillary dysentery or even after a major surgical operation.

Loss of weight, fatigue, irritability or anxiety symptoms in men with a negative sigmoidoscopy but with cysts in their stools, responding to anti-amœbic treatment, suggest that constitutional symptoms, with or without clinical hepatitis, may predominate when the seat of infection is chiefly cæcal, though when the rectum is involved dysentery and pain are manifest.

All dysenteric patients were sigmoidoscoped on admission to hospital and again before discharge. Our only preparation was for the patient to defæcate before examination. This simple routine was of great diagnostic value, especially in the apparently cured. Thus, many cases of acute bacillary dysentery after sulphaguanidine were found to harbour unsuspected chronic amœbic ulceration in the rectum. Although this drug successfully eliminated an acute bacillary infection from the bowel it made the microscopic detection of entamœbæ more difficult afterwards. We felt that sulphaguanidine had, maybe, some specific anti-amœbic action, enough to rid the bowel contents of amœbæ and cysts yet not enough to heal, for vegetative forms remained in the ulcers.

Treatment.—Treatment is begun at once after diagnosis and the detailed routine of a full consecutive course must be followed. Although various doses and combinations of drugs have been advocated in the past, treatment now is standardized. All patients, irrespective of the stage of their disease, are put to bed and given a course of emetine bismuth iodide by mouth, chiniofon by bowel and carbarsone. Emetine hydrochloride is reserved solely for patients with symptoms, intestinal or constitutional, or with vegeta-

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The injections are followed without a break by the course of EBI, twelve consecutive daily doses of 3 grains by mouth, together with retention enemata of chiniofon. EBI is normally dispensed in gelatin or sugar-coated capsules both of which render disintegration and absorption uncertain. We gave it direct as powders either in a spoonful of jam or on the back of the tongue with a drink. EBI is customarily administered at night with a harbiturate sedative to allay the nauseating effect, but we found it was well tolerated and toxic effects need not be anticipated. The stools should always be inspected as a control of assimilation; they are dark from the bismuth in the compound.

Chiniofon enemata, consisting of 7 oz. of 2½% solution daily for these twelve days, were given simultaneously with EBI. (Synonyms: yatren, quinoxyl, quiniolulpham.) To help to retain each enema for at least six hours the foot of the bed is raised on 8 in. blocks. The patient should lie in turn, for half an hour each on his left side, back and right side. This drill keeps him recumbent but has no other particular value, for we have shown by X-rays that enemata reach the cæcum from the supine position. Patients will often tolerate with benefit a gradual increase both in volume and strength of the enemata. Towards the end of the EBI course some diarrhœa is common and upsets retention unless an alkaline bowel washout is given before. In a busy ward the sterilization of apparatus must be supervised to prevent cross infection of bacillary exudate.

Finally, for a further twelve days, carbarsone (or stovarsol) was given, 4-grain tablets twice daily, to eradicate cysts, and the patient was then allowed up.

We had a small experience of Kurchi bismuth iodide at a time when EBI was scarce but were not convinced that it replaced EBI as an active amœbicide.

Emetine resistance.—One has learnt that interruption of treatment is a cogent cause of chronicity and relapse. Its relative incidence is high, for example, among doctors, because we are sometimes too impatient to undergo the prescribed full course and are inclined to modify it to our convenience. In one's earlier experience, when treatment was not standardized and soldiers were denied the proper drugs through short supply, relapses were common and many apparently intractable cases were invalidated home. We now realize that few of these so-called emetine-fast cases had a completed course of treatment controlled in hospital. Latterly it became rare, except for operational reasons, to evacuate any patient with chronic amœbiasis. Emetine resistance clearly is more apparent than real. There are perhaps exceptional cases which do not at first respond to standard treatment, yet even these will generally react to a second course repeated after an interval, when penicillin and sulphasuxidine may be needed to clear secondary colonic infection.

CONCLUSIONS

The continuous sequence of treatment is all-important. Hypodermic emetine deals only with initial symptoms; by itself it does not cure. EBI (by mouth) and chiniofon (enemata) are possibly the keystones of treatment. Carbarsone should clear residual cysts. The twelve-day periods in therapy are arbitrary; they may be prolonged but never reduced. Bed-rest is essential for the first two to three weeks but diet restriction and purges are not. Convalescence for three weeks is desirable, followed by readmission to hospital for six daily stool tests of cure and final sigmoidoscopy.

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interval of two weeks during which daily retention enemata of sulphasuxidine were given. He relapsed after seven months, but has responded again to another course of treatment.

We have treated 7 other patients with ulcerative colitis and proctitis. All showed a satisfactory response, but 2 had persistent granularity in the lower part of the rectum—one after four courses of treatment. Only one patient had a ribbon-like colon radiologically, and there was no change in this appearance after treatment, although ulceration had healed. These patients were definitely improved, but one cannot claim that they were cured.

Our clinical experiences are open to the criticism that they did not always have strict bacteriological control. Occasionally we have been able to isolate penicillin-sensitive streptococci and staphylococci from the dysenteric cases, and in 2 cases of ulcerative colitis penicillin-sensitive staphylococci have been found.

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of anæsthetic, from which they recover, to be narcotized once more by another few injections of emetine—but not killed.

In our experience emetine, or EBI, must always be given *every* day for at least ten days, better for twelve days. In early, acute cases this is usually enough to rid the body of the amœbæ, but a few days (without interval) of carbarsone t.d.s. makes matters more certain.

The stressing of the importance of continued daily treatment is very important in India, where so many doctors seem to be completely ignorant of its significance.

The chronic cases with cysts require adjuvant treatment with quinoxyl retention enemata. Our practice was to give these on the 2nd, 3rd, 9th, 10th, and 11th days of the emetine or EBI administration.

During the latter part of the war we could not obtain quinoxyl, and we substituted carbarsone, 4 times daily for 5 days, beginning it on the 8th day of emetine injections, or enterovioform enemata daily for ten days.

In the last two years we have dealt with 130 cases of this kind, many of whom have had previous inadequate emetine treatment, and many others suffering from much malnutrition through famine.

Average number of days in hospital fifteen, deaths six. The remainder went home clinically cured and free from amœbæ to pathological examination. There were 4 cases of arsenical dermatitis.

No case was considered "cured" until negative to five successive examinations of feces, and latterly to sigmoidoscopy also. Presence of degenerated leucocytes is treated as positive, even though amœbæ are not seen.

The rectum in amœbiasis.—During the last few years we have seen 10 cases of amœbic disease of the rectum. 5 of these were proctitis with fistule, the fistule being very deep, opening into the rectum about 3 in. from the anus. Emetine, as always most effective in extra-colonic amœbic disease, clears up the amœbic infection, but colostomy also is always required. 2 cases refused colostomy and never healed. 3 cases had colostomy and plastic rectal operations, and were healed; one of these afterwards broke down three years after the closure of the colostomy. 5 cases had fibrosis of the rectum. In these 5, the mucous membrane was teeming with active amœbæ. After a full course of emetine, very gradual dilatation was tried, and was effective in 3 cases. Permanent colostomy was necessary in the other 2 cases, in which the rectum for 3 or 4 in. would scarcely admit a pencil, nor could it be safely dilated.

We have also had 4 cases of burrowing abscesses of the perineum and buttock, in which amœbæ were present. These had long histories of ineffective treatment. They all cleared up with emetine and excision of the walls of the abscesses in a surprisingly short time.

(Major R. M. S. McConaghey reviewed 19 similar cases, nearly all in China, and only one from India. See *Indian med. Gaz.*, 1945, 80, 79.)

It is my opinion that all cases of carcinoma of rectum in the tropics should be tested for amœbæ before operation and/or radium treatment is embarked upon.

Bacillary and Amœbic Dysentery Together.

Speaking as a patient who suffered during the 1914-18 war with a combination of both diseases, one (amœbic) of which was only discovered on my demobilization in 1920, I am convinced that there are many cases who have both infections, and in whom the acute stage of one infection has lit up the other.

Colonel J. R. Davidson tells me that in the recent war it became the custom to treat all dysentery cases with sulphaguanidine in the line, and only evacuate them if there was no adequate effect in twenty-four to forty-eight hours.

If these cases proved at the base to have amœbæ, the routine then was (for all cases, acute and chronic):—

Emetine 1 grain daily for 6 days	} 12 days— {	Yatren 5th—12th day
EBI 3 grains daily for 6 days		8 oz. 2½% rel. enema
		Days 13—14 Yatren enema only
		Days 15—24 Carbarsone 0.25 grammes twice daily

Only 3% of chronic cases relapsed after this treatment, and no acute cases. This for acute cases is extremely thorough treatment, and is what I consider a full course for

a chronic case. If you have the drugs, and the patients under your control, it is certainly ideal as far as thoroughness is concerned. The routine exhibition of a sulpha drug for the first two days of all dysenteries is probably to be recommended. It can do nothing but good even in a purely amoebic case.

Bacillary dysentery.—In fresh cases of bacillary dysentery, of not more than three days duration, the sulphonamide drugs are, as we all know, brilliantly successful. But so are several other treatments.

In more chronic cases, however, the situation is far more serious. Hitherto the problem of chronic bacillary dysentery has been a serious one; but to the surprise of many people it has been found that sulphamezathine and sulphaguanidine, and even sulphapyridine, produce remarkably good results with a high percentage of cures in chronic cases.

In 1945 we treated 85 cases of bacillary dysentery, and many of these were very weak on admission, some of them having a choleraic type of dysentery. Most were infected with Flexner bacilli, and many were suffering from a degree of starvation owing to war conditions. The standard treatment was:

Sulphapyridine or sulphamezathine, 3 grammes, then 1 gramme four-hourly for two days, followed by
Sulphaguanidine, 1 gramme four-hourly for two days.
(Sulphaguanidine, 3 grammes four-hourly, the usual dose, caused toxic symptoms in many cases.)

In this series there were 8 deaths, nearly 10%, a far better result than we have had in a similar series of emaciated cases with any other treatment. Strangely enough we have found sulphapyridine more effective, and apparently less toxic, than sulphaguanidine for bacillary dysentery.

With regard to the complications of bacillary dysentery, the one which is made little of in most textbooks, but is very common in S. India, is chronic peritonitis with massive serous effusion. This is very resistant to treatment, and if the patients are aspirated they soon fill up again. It is said that omentopexy has been followed by very bad results.

Tuberculous disease of the colon, etc.—In South India we have had a large number of cases of hyperplastic disease of the colon due to the tubercle bacillus, also 8 cases of Crohn's regional "ileitis" in the colon.

For these conditions we have found no drug to be of the slightest use. We have never used sulphasuxidine, however. (Amoebic and other infections are, of course, excluded by full pathological investigations).

The treatment must be surgical, and ileocolic anastomosis as well as excision of the tuberculous colon must be done at one sitting. If ileotransverse anastomosis is done and the tuberculous colon (usually caecum) is left, the patient's health may improve, but the colon nearly always gets worse, and eventually requires a more extensive operation for its removal.

In 51 cases, there were 4 deaths, no deaths in the last 30 cases, perhaps owing to the sewing of the anastomosis in 3 layers.

If the appearance at operation is quite certainly that of Crohn's disease, anastomosis alone may be done; the disease progresses much more slowly than tuberculous trouble, and does not tend to get adherent, to form abscesses, etc.

Diagnosis between the two is helped by the sedimentation test. Average figures for TB, 0 ... 56 ... 70. Average figures, Crohn, 0 ... 26 ... 38.

Mr. C. Naunton Morgan: It is probable as an aftermath of world-wide war, that both bacillary dysentery and certainly amoebiasis occurring in the United Kingdom will give rise to difficulties and misdiagnosis unless the protean nature of the latter disease, and especially the fact that amoebiasis may remain latent without symptoms for many years, are borne in mind.

Emetine has proved of great value in both the diagnosis and treatment of amoebiasis, as this disease presents itself to the surgeon.

Amoebic granulomata (amoeboma) occurring in the colon and rectum in the Eastern theatres of war sometimes made the differential diagnosis of these tumours from carcinoma

difficult, especially since both malignant disease and amœbiasis may coexist. In M.E.F., of 21 patients with malignant lesions of the colon and rectum referred to the rectal centre, no fewer than 12 were diagnosed as bacillary or amœbic dysentery, and in 5 of these cases the carcinoma had been at first mistaken for an amœboma. In 7 cases bacillary or amœbic dysentery were found associated with a carcinoma.

Apart from biopsy, which may be fatally misleading unless a representative piece is removed for section, emetine is of great value in differential diagnosis. In the large majority of cases an amœboma melts away in a dramatic manner following the administration of a course of emetine injections and the diagnosis is established even though the amœba, which may be lurking in the depths of the tumour, cannot be isolated. However, on very rare occasions when destruction of the bowel wall has progressed beyond the stage at which anatomical recovery is possible, surgical intervention becomes necessary, not only to restore the patient to health, but more often because malignant disease cannot be excluded with certainty. A tumour of the cæcum with proven amœbiasis was excised because, though the mass diminished in size after several courses of emetine, etc., it still remained. At operation and on macroscopic examination the cæcal tumour was thought to be an amœboma, but section showed it to be a carcinoma.

The dangers of abdominal and rectal operations in the presence of amœbiasis or bacillary infection are now generally recognized so that in suspected cases, when there is no indication for urgent operation, specific therapy must be given before surgical intervention.

Amœbic typhlitis and acute appendicitis caused anxiety in the diagnosis of the acute abdomen. However, when acute appendicitis is diagnosed early, and especially when there are signs and symptoms indicating rapid extension of intraperitoneal infection or obstruction to the appendix lumen, even though amœbic infection is present, immediate operation must be performed. If typhlitis is found at operation, even though amœbic infection is not proven, but probable, it is wise to commence specific therapy at once.

Invasion of the skin at the site of the operation wound may be the first indication of the presence of amœbiasis. The skin lesions also respond rapidly to emetine.

It is worthy of record that an amœbic ulcer of the anal canal skin, an amœbic fissure-in-ano, has been observed getting larger during the administration of carbarsone, and fading away soon after emetine was exhibited.

Both bacillary and amœbic infection may be present at the same time, and on sigmoidoscopy the diffuse inflammation of the mucosa in the former may overshadow the tiny lesions of amœbiasis. In such cases, repeated sigmoidoscopy after the administration of sulphaguanidine for about a week will reveal the two-edged nature of the infection.

Though the sigmoidoscopic appearances of amœbic and bacillary dysentery are described as being clear cut, this is not the case, and tiny localized ulcers may occur in otherwise normal mucous membrane, due to Flexner infection; whilst on the other hand, diffuse granular proctitis may be amœbic in origin. The administration of emetine and/or sulphaguanidine may be the only method of establishing a diagnosis.

Succinylsulphathiazole in the Surgery of the Rectum and Colon.

Succinylsulphathiazole (sulphasuxidine) introduced by Poth in 1942, reduces the bacterial count of the intestinal contents and also makes the faeces less bulky and of a slightly sticky consistency, so allowing their removal from the lumen with less likelihood of contamination. In addition, the drug appears to have a slightly laxative effect. Increase of bleeding from a carcinoma has been observed by Firor and others, after five days' administration of the drug.

Though the dosage recommended in terms of body-weight, usually 8 to 10 grammes daily, was used in 1942 in M.E.F., investigation of our cases by Mackenzie at the 15th Scottish General Hospital showed that the breakdown of this drug is unlikely to exceed 5%, and we came to the conclusion that 20 grammes daily for four days, followed by 20 grammes in one dose on the day of the operation was the most efficient dosage. Results with 5 grammes, 10 grammes and 20 grammes dosage were compared. It was found that culture of a scraping of the carcinomatous ulcer grew no *B. coli* when a 20-grammes dose was used for five days, and that in the case of ileostomy for complete colectomy and excision of the rectum, *B. coli* in the small gut had been laid low by succinylsulphathiazole.

When a preliminary colostomy has been performed, succinylsulphathiazole 20 grammes in 6 oz. of half strength mucilage is inserted into the excluded bowel daily for ten to fourteen days following lavage.

Sulphasuxidine was used before operation in 33 cases, and in only 1 was there evidence of intraperitoneal infection. An abdominal abscess developed insidiously and without fever, following a combined excision of the rectum, bursting into the general peritoneal cavity on the eleventh day. This patient quickly recovered after drainage of the abdominal cavity. Apart from this one complication, the smooth convalescence following operation was striking.

Sulphonamides which control the intestinal flora are important adjuvants in the surgery of the large bowel, but though the number of organisms in the intestine may be controlled, these drugs do not allow any relaxation in the care and established principles of the surgery of the colon and rectum.

Mr. A. Dickson Wright: With the discovery of sulphonamides and their amazing properties the long-dreamt-of possibility of sterilizing the colonic contents became a practical possibility. The difficulty was that the sulphonamides were absorbed in the small intestine and if they were wanted for colon sterilization introduction by enema was necessary. This was tried and had some success, but it was an uncertain method of administration; it was necessary to have a compound which would not be absorbed when taken by mouth and so would be thoroughly mixed with the faeces and exercise a uniform sterilizing action on the contents. This was not difficult to achieve with all the chemical linkages available and neoprontosil, sulphaguanidine, sulphasuxidine and sulphathalidine were all evolved in turn, each with a diminishing absorbability but unimpaired bactericidal action.

Having achieved the sterilization of the colonic contents the way was laid open to the immediate cure of certain hitherto dangerous diseases such as the bacillary dysenteries and to the mitigation of many other ulcerative diseases in which secondary bacterial infections from the faeces were an important secondary effect. In addition to the sterilization of the faeces these also became mushy in consistency and much less irritating to conditions such as diverticulitis and recent suture lines in the bowel.

The following conditions can only benefit from sterilization of the faeces: Amœbic dysentery, ulcerative colitis, diverticulitis, Crohn's disease and perirectal suppurations.

The operative surgery of the colon is robbed of all infection fears by the administration for five days of 24 grammes daily of sulphasuxidine or 12 grammes of sulphathalidine, given in divided doses at three-hourly intervals. Five days will not suffice if there is obstruction or abscess formation present. With this premedication the whole colon and not only the right half is available for one-stage resection with shorter time in hospital and no unpleasantness of temporary colostomies and Mikulicz resections.

Mr. Alan H. Hunt: My communication deals briefly with the effect of sulphasuxidine in reducing the incidence of peritonitis when given before major intraperitoneal operations on the colon and rectum.

The figures are derived entirely from Mr. Lawrence Abel's Clinic at the Royal Cancer Hospital, and I am greatly indebted to him for allowing me to analyse these cases and to present the tabulated results at this meeting.

At the Cancer Hospital we tend to get cases of a desperate nature, sent there from somewhere else and as a last hope. The fatality rate is thus not indicative of what is disclosed by an analysis of a wider range of cases: but I have limited the analysis to Cancer Hospital patients for the very good reason that we thus deal with two series of consecutive cases in which the operative technique, theatre facilities, nursing, etc., have been unchanged throughout the period of analysis.

There is only one factor which differs between the two groups of cases—the administration of sulphasuxidine pre-operatively in the second group. (There is, of course, penicillin, which became available in reasonable quantities in 1944. But we would not expect this drug to have an appreciable effect on peritoneal infections arising from faecal contamination.)

Table I shows the results before the introduction of sulphasuxidine in September 1943. I have divided the cases of carcinoma of the rectum into the four stages: Stage I limited to the rectum, II extending beyond the rectum, III with regional lymphatic metastases and IV with distant metastases. 11 of these 78 patients died, 2 of diffuse peritonitis, 1 of intraperitoneal abscess, 4 with localized peritonitis evident post mortem, and 4 of other causes.

Of 12 other cases, 4 died, 2 with diffuse and 2 with localized peritonitis.

TABLE I.—1939—AUG. 1943: BEFORE INTRODUCTION OF SULPHASUXIDINE.

Carcinoma of rectum Abdomino-perineal excision	Stage	No.	Av. age	Deaths	Age	Cause of death
	I	8	53	—		
	II	39	57.5	6	55	Pneumonia
					62	Pneumonia with local peritonitis
					61	Pneumonia with local peritonitis
					74	Heart failure with local peritonitis
					51	General peritonitis
					55	Suicide
	III	21	55	3	62	Uræmia
					54	General peritonitis
					57	Heart failure with local peritonitis
	IV	10	51	2	51	Local peritonitis with ac. dil. stomach
					62	Heart failure
Totals		78		11	Average stay in hospital of 67 survivors was 51 days	
Hartmann's operation	...	4	60	1	73	Heart failure and uræmia with local peritonitis
Colonic resection and anastomosis		6	62	3	88	Local peritoneal abscess
					60	Diffuse peritonitis
					74	Diffuse peritonitis
Palliative colonic anastomoses		2	60	—		
Totals		90		15	At death: Diffuse peritonitis ... 4 Local peritonitis ... 7	

Table II shows the results in the second group, after the preoperative administration of sulphasuxidine had become an established routine. The dose has been 50 grammes, 10 grammes given daily for five days.

TABLE II.—1944-45: AFTER INTRODUCTION OF SULPHASUXIDINE
10 gm. DAILY FOR 5 DAYS BEFORE OPERATION.

Carcinoma of rectum Abdomino-perineal excision	Stage	No.	Av. age	Deaths	Age	Cause of death
	I	5	47	1	71	Pulmonary embolus
	II	20	59	2	72	Pulmonary embolus
					62	Heart failure
	III	20	60	1	73	Pneumonia
	IV	5	61	—		
		1	66	—		
Carc. paracophoron A-P with Wertheim	Totals	51		4	Average stay in hospital of 47 survivors was 40.5 days	
Hartmann's operation and excr. with extra-peritoneal anastomosis		5	47	2	60	Heart failure with multiple metastases (stage iv)
					63	Pylonephritis and uræmia
Colonic resection and anastomosis		14	55	2	44	Obstruction from adhesion to intraperitoneal deposit
					63	Pneumonia
Palliative anastomoses	...	5	56	1	41	Extensive malignant disease
Totals		75		9	At death: Diffuse peritonitis ... 0 Local peritonitis ... 0	

Here there were but 4 deaths in 51 abdomino-perineal resections, 2 due to pulmonary embolism, 1 to heart failure and 1 to pneumonia. There was no peritonitis.

Of the remaining 24 miscellaneous cases in this table, 5 died, and again intraperitoneal infection was conspicuous by its absence.

To summarize, of the 90 cases undergoing major intraperitoneal operations on the colon before the introduction of sulphasuxidine, 15 died (a fatality rate of 16.5%), and of these 4 had diffuse and 7 localized peritonitis at death. Of the 75 cases operated on after the introduction of sulphasuxidine, 9 died (a fatality rate of 12%), and of these none had any intraperitoneal infection.

The length of convalescence after abdomino-perineal resections is a good indication of the extent of wound infection. Without sulphasuxidine, the average stay in hospital after operation was 51 days; with sulphasuxidine, 40.5 days. This reduction of ten days seems to be significant.

Section of Obstetrics and Gynæcology

President—Professor F. J. BROWNE, M.D.

[November 16, 1945]

DISCUSSION ON PLACENTA PRÆVIA

Mr. C. H. G. Macafee, in opening the discussion, described the policy of the Royal Maternity Hospital, Belfast. In 1937 it was decided to allocate the three common emergencies to three members of the visiting staff. The care of all cases of antepartum hæmorrhage was allocated to him. His remarks were based on 191 cases (including 24 private cases) from 1937 until September 30, 1945. There was one maternal death (0.52%) and 42 stillbirths and neonatal deaths (22%). When the foetal mortality was corrected by the elimination of abnormalities such as anencephaly from the stillbirths and of gastro-enteritis from the neonatal deaths it was only 18.8%.

In any case of placenta prævia the attendant who saw the patient first had a great responsibility. He must recognize that, unless in the exceptional event of a serious hæmorrhage, the patient should be removed to an institution without any vaginal examination being made. The fact that only a few patients in this series had been examined before admission must have had an important influence on the results.

The main objectives in dealing with placenta prævia were to reduce foetal mortality without unfavourably affecting the maternal condition and to keep an open mind concerning treatment. One of the main causes of foetal mortality in placenta prævia is prematurity. This can be reduced only by carrying on the pregnancy to as near full term as possible.

In support of his opinion that there is a definite place for expectant treatment in this complication he submitted the following arguments:

(1) A severe initial hæmorrhage rarely occurs apart from vaginal manipulations. The number of primigravidae, and indeed multiparæ, who proceed to full term with extreme degrees of placenta prævia without hæmorrhage is striking.

(2) Some patients have a sharp but not severe hæmorrhage at 30 to 34 weeks. Later the placenta can be palpated inside the os without provoking further bleeding, this being due to infarction of the separated area.

(3) Repeated hæmorrhages have occurred while in hospital without embarrassing mother or baby. Many patients carry out their own expectant treatment by ignoring small hæmorrhages, until one occurs which alarms them.

The attitude that a placenta prævia is not an obstetrical emergency which must receive active treatment at the first hæmorrhage has meant that the infant's chance of survival is much enhanced. Approximately 42% of the stillbirths or neonatal deaths occurred in the first two years under review, whereas in 1944 there were only three such deaths (16.6%) and in the first nine months of 1945 one death (6.4%).

The type or degree of placenta prævia has an important influence on treatment. He appealed for the removal of the terms "lateral", "marginal" and "central" from obstetric literature, the last two being inconsistently used by medical writers. Browne's classification if adopted universally would ensure uniformity. This classification, with the use of the term "type" instead of "degree", has been followed in the present paper.

Mr. Macafee went on to say that placenta prævia is usually a much larger and thinner placenta than one normally situated, and frequently has an excentric insertion of the cord. Insertion of the umbilical cord in relation to the separated area of the placenta is important and accounts for a certain unavoidable foetal mortality. If the cord is inserted at the lower edge of the placenta where the separation occurs or, if it has a velamentous insertion in this area, the child is unlikely to survive after the initial hæmorrhage.

The decision regarding a vaginal examination demands the careful consideration of an experienced obstetrician. With few exceptions a vaginal examination has been performed on all cases in this series, but only after all preparations were complete for immediately carrying out the appropriate treatment for the individual case, therefore the examination has been postponed until the termination of expectant treatment and is then made with the patient on the operating table. The cervix and the vagina should, of course, be inspected *per speculum* after the first hæmorrhage to exclude local causes of bleeding.

TABLE I.—1939—AUG. 1943: BEFORE INTRODUCTION OF SULPHASUXIDINE.

Carcinoma of rectum Abdomino-perineal excision	Stage	No.	Av. age	Deaths	Age	Cause of death
	I	8	55	—		
	II	39	57.5	6	55	Pneumonia
					62	Pneumonia with local peritonitis
					61	Pneumonia with local peritonitis
					74	Heart failure with local peritonitis
					51	General peritonitis
					55	Suicide
	III	21	55	3	62	Uræmia
					54	General peritonitis
					57	Heart failure with local peritonitis
	IV	10	51	2	51	Local peritonitis with ac. dil. stomach
					62	Heart failure
Totals		78		11	Average stay in hospital of 67 survivors was 51 days	
Hartmann's operation	...	4	60	1	73	Heart failure and uræmia with local peritonitis
Colonic resection and anastomosis		6	62	3	38	Local peritoneal abscess
					66	Diffuse peritonitis
					74	Diffuse peritonitis
Palliative colonic anastomoses		2	60	—		
Totals		90		15	At death: Diffuse peritonitis ... 4 Local peritonitis ... 7	

Table II shows the results in the second group, after the preoperative administration of sulphasuxidine had become an established routine. The dose has been 50 grammes, 10 grammes given daily for five days.

TABLE II.—1944—45: AFTER INTRODUCTION OF SULPHASUXIDINE
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To summarize, of the 90 cases undergoing major intraperitoneal operations on the colon before the introduction of sulphasuxidine, 15 died (a fatality rate of 16.5%), and of these 4 had diffuse and 7 localized peritonitis at death. Of the 75 cases operated on after the introduction of sulphasuxidine, 9 died (a fatality rate of 12%), and of these none had any intraperitoneal infection.

The length of convalescence after abdomino-perineal resections is a good indication of the extent of wound infection. Without sulphasuxidine, the average stay in hospital after operation was 51 days; with sulphasuxidine, 40.5 days. This reduction of ten days seems to be significant.

there was the greatest co-operation between the obstetrician, residents and nursing staff. Given these conditions, equally good results can be achieved, using methods which may vary greatly as regards the details of obstetric treatment.

My own cases of placenta prævia were examined under a general anæsthetic with complete asepsis. The vagina was ironed out, the whole hand introduced, and the index finger passed through the cervix and the position of the placenta ascertained, care being taken to produce as little bleeding as possible. If the presenting part were a vertex, easily palpated with little disturbance of the placenta, the membranes were ruptured and nothing more done. If the presenting part were a flexed breech, the os two fingers dilated and the breech easily reached without producing much hæmorrhage, the membranes were ruptured and a foot drawn down. This treatment was mostly used where the babies were either small or dead. If after rupturing the membranes, or subsequently, a severe hæmorrhage occurred, the vagina was plugged with rolls of 6-in. gauze soaked in Dettol 5%, from 3 to 5 rolls, 6 yards in each being used, and a pad and tight binder applied. The plugging was retained the minimum time possible.

Table A gives the main results in 139 consecutive cases treated at Queen Charlotte's Hospital by all members of the staff prior to 1933. All methods of treatment were used, including vaginal plugging.

Table B shows my own series of cases similarly analysed.

TABLE A.—139 CONSECUTIVE CASES ENDING 1933

Maternal mortality rate 6.47%.			Stillbirth rate 52.5%.			Morbidity rate 14.7%.		
Complete placenta prævia—Type 3			Marginal placenta prævia—Type 2			Lateral placenta prævia—Type 1		
Total	Maternal deaths	Stillbirths	Total	Maternal deaths	Stillbirths	Total	Maternal deaths	Stillbirths
31	3 (19.3%)	22 (71%)	48	3 (6.25%)	34 (71%)	60	Nil	17 (28.3%)
All types of treatment were used.								

TABLE B.—143 CONSECUTIVE CASES (1933-1938)

Maternal mortality rate 1.4%			Stillbirth rate 58.7%			Morbidity rate 15.4%		
Complete placenta prævia—Type 3			Marginal placenta prævia—Type 2			Lateral placenta prævia—Type 1		
Total	Maternal deaths	Stillbirths	Total	Maternal deaths	Stillbirths	Total	Maternal deaths	Stillbirths
12	Nil	2 (16.6%)	79	2 (2.5%)	53 (64.6%)	52	Nil	29 (55.8%)

TABLE C.—ANALYSIS OF METHODS OF TREATMENT (1933-1938)

Method of treatment	Number of cases	Maternal deaths	Stillbirths
Artificial rupture of membranes and binder	54	Nil	21 (39%)
Bringing down leg	15	Nil	14
Cæsarean section	9	Nil	Nil
Cæsarean section after plugging	6	Nil	1
Plugging with rupture of the membranes and binder	59	2	39 (66%)

I am not an ardent supporter of vaginal plugging in the treatment of placenta prævia, though I think there are still occasions when it is difficult to avoid it. I am opposed to its use in domiciliary practice, but in hospital, with full surgical asepsis, I think it still has a place, though an occasional one, in the treatment of placenta prævia. This series shows that, in spite of opinion to the contrary, vaginal plugging properly carried out can control severe hæmorrhage in placenta prævia cases, and that sepsis when it occurs, is very moderate and can be ignored. In this series, the sepsis rate following plugging was less than 1% greater than the rate obtained in 143 consecutive cases treated by all members of the staff and by all known methods. In this series an attempt was made to get good results by obstetric methods and without doing a large number of Cæsarean sections, and I think it succeeded. Looking back on these cases I think I made four mistakes: (1) Many of them could have been left after admission until a severe hæmorrhage occurred, thus improving the foetal mortality rate. (2) All cases at the original examination should have been on the operating table of the theatre, so that a Cæsarean section could have been carried out immediately, if necessary. (3) I can now see no advantage in using dilators to establish the position of the placenta in primigravidae with a closed cervix. If a sharp hæmorrhage occurs in such cases they are best treated by a Cæsarean section, without disturbance of the placenta. (4) In another such series of cases I would plug the vagina much less frequently, and do many more Cæsarean sections.

A vaginal examination is essential because:

- (1) It is not possible to diagnose a placenta prævia on the character of the bleeding.
- (2) The diagnosis of placenta prævia should not be made unless the placenta has been felt in the lower uterine segment.
- (3) Only when the type of placenta prævia is determined can one decide upon the best method of treatment.

RESULTS OF VARIOUS METHODS OF TREATMENT

Treatment	No. of cases	Stillbirths or died	%
Artificial rupture of membranes	54	7	13
A.R.M. and Willetts forceps	21	9	42.9
Version	23	18	78.3
Cæsarean section	79	2	2.5
Breech	6	5	83.3
None	8	1	12.5

The one maternal death followed a Cæsarean section, and was due to a staphylococcal septicæmia; a maternal mortality rate for Cæsarean section of 1.27%.

Type I can usually be dealt with by rupture of the membranes.

In Type II, if the placenta lies anteriorly, artificial rupture of the membranes is usually sufficient, but if the placenta is in the posterior position a Cæsarean section is indicated.

Type III in the series was associated with the highest foetal mortality, due to the fact that hæmorrhage occurs at a much earlier period of gestation.

Type IV necessitates Cæsarean section.

In the light of the excellent results recently published, the attitude towards maternal and foetal mortality associated with placenta prævia must be revised. This mortality has been regarded as inevitable in the past. He believed it could be radically reduced. If the policy outlined could be adopted more generally he felt sure that in less than ten years results would be forthcoming which would completely eclipse the figures in this series.

The results presented were not due to the efforts of any one person but to co-operation between many: general practitioners, hospital residents and nursing personnel, blood transfusion service, anaesthetists, pædiatric department and the patient herself.

Mr. Leonard Phillips: In 1933 a scheme of allocation of cases was instituted at Queen Charlotte's Hospital, and from 1933-38 it was my privilege to treat most of the cases of placenta prævia which were admitted to the hospital. A series of 143 consecutive cases was treated with a maternal mortality rate of 1.4%.

The first factor which has helped to reduce the maternal mortality rate is the better condition in which cases are now admitted to hospital. Most practitioners now realize that cases of placenta prævia can only be treated satisfactorily in hospital, where asepsis, blood transfusions, skilled nursing and specialized obstetric help are available.

The second factor in securing good results is blood transfusion. I consider that the most important factor in securing my own results was blood transfusion. Many cases received one transfusion and some cases two or three transfusions. The majority of deaths in placenta prævia cases occur as a result of hæmorrhage. In any modern, well-staffed and well-equipped hospital a death from hæmorrhage should be rare.

The third factor which has helped to reduce the maternal mortality rate is the greatly extended scope of Cæsarean section. The following types of cases are best treated by Cæsarean section:

(1) All cases in which, at the first examination under anæsthetic, the placenta is found to cover completely the os which is one to two fingers dilated, and in which the presenting part cannot be reached without separating the placenta and causing sharp hæmorrhage.

(2) All cases in which a sharp hæmorrhage has occurred in a primigravida with an undilated cervix.

The increased consideration now given to the claims of the child is another reason for the extended use of Cæsarean section. These are the days of one-child marriages or spaced children, the child may be the first after ten years of marriage, and the mother may demand a Cæsarean section; we are all very much aware of the psychological damage to the mother following the loss of a child for which she has waited many years, and finally, the methods now employed in rearing premature babies have greatly improved. If therefore the fœtus is 36 weeks mature and alive at the first examination under anæsthetic, there is usually a strong case for Cæsarean section, apart from the maternal indications.

The fourth factor responsible for improved results is team work. In my own cases

unless there is severe hæmorrhage. All patients, however slight the hæmorrhage, are advised to remain in hospital until confinement.

The chief justification for expectant treatment is that it gives the fœtus a chance of reaching maturity. For cases of placenta prævia, it is now established that Cæsarean section offers the best chance for the fœtus and it is taking an increasingly important place in the treatment of these cases.

We have found little difficulty in persuading patients to remain in hospital for the long periods, eight or even ten weeks, that may be necessary. Shortage of hospital beds should not be admitted as a reason for not giving expectant treatment. Antepartum hæmorrhage is one of the gravest of all obstetric emergencies and requires the best treatment.

TABLE II—MATERNAL AND FETAL MORTALITY IN ANTEPARTUM HÆMORRHAGE

				(Excluding extra-placental lesions)			
Mothers	517	Mothers	498
Maternal deaths	14	Maternal deaths	14
Maternal mortality	2.7%	Maternal mortality	2.8%
Infants	520	Infants	501
Infant deaths	192	Infant deaths	190
Infant mortality	36.9%	Infant mortality	37.0%

TABLE III—MATERNAL AND FETAL MORTALITY IN ANTEPARTUM HÆMORRHAGE CLASSIFIED ACCORDING TO THE NATURE OF THE LESION

Placenta Prævia :				Antepartum Hæmorrhage of Uncertain Origin :			
Mothers	140	Mothers	285
Maternal deaths (1 died undelivered)	4	Maternal deaths	1
Maternal mortality	2.9%	Maternal mortality	0.4%
Infants	138	Infants	288
Infant deaths (in 33 the leg was pulled down)	72	Infant deaths	80
Infant mortality	52.2%	Infant mortality	27.8%
Accidental Antepartum Hæmorrhage :				Antepartum Hæmorrhage from Extra-placental Lesions :			
Mothers	73	Mothers	19
Maternal deaths (3 died undelivered)	0	Maternal deaths	0
Maternal mortality	12.3%	Infants	19
Infants	75	Infant deaths	2
Infant deaths	38	Infant mortality	10.5%
Infant mortality	50.7%				

TABLE IV.—METHODS OF TREATMENT IN CASES OF PLACENTA PRÆVIA

Cæsarean section	38	Willet's forceps	36
Maternal deaths	1	Maternal deaths	2
Maternal mortality	2.6%	Maternal mortality	5.6%
Infant deaths	7	Infant deaths	17
Infant mortality	18.4%	Infant mortality	47.2%
Bringing down a leg	39	Artificial rupture of membranes	11
Maternal deaths	0	Maternal deaths	0
Infant deaths	38	Infant deaths	4
Infant mortality	97.4%	Infant mortality	36.4%

TABLE V.—DEGREE OF PLACENTA PRÆVIA

First degree	53	Third degree	25
Maternal deaths	0	Maternal deaths	0
Infant deaths (out of 52)	23	Infant deaths (out of 24)	12
Infant mortality	44.2%	Infant mortality	50%
Second degree	51	Fourth degree	10
Maternal deaths	4	Maternal deaths	0
Maternal mortality	7.8%	Infant deaths	3
Infant deaths (out of 50)	33	Infant mortality	30%
Infant mortality	66%				

Degree of placenta prævia not ascertained 1

TABLE VI.—PLACENTA PRÆVIA (1936-1945)

	1936	1937	1938	1939	1940	1941	1942	1943	1944	1945
Total	11	10	7	4	6	2	7	5	4	10
Maternal deaths	0	1	0	0	0	0	0	0	0	0
Infant deaths	0	4	6	1	2	1	3	0	0	1
(twin)										
Maternal mortality	1 out of 66					= 1.5%				
Infant mortality	24 out of 67					= 35.6%				

Professor James Young said that the main conclusion from Mr. Macafee's paper was the considerable reduction in fetal mortality which could be obtained by the extension of the expectant treatment of placenta prævia and without any addition to the maternal risk. Professor Young recorded the results of ten years' experience at the British Post-

Miss Josephine Barnes (*Abridged*): It is proposed to deal with the subject of placenta prævia in relation to the general problem of antepartum hæmorrhage. Between the years 1927 and 1944 inclusive, 538 cases of antepartum hæmorrhage have been admitted to the Obstetric Hospital, University College Hospital. These cases are now classified into four groups as follows:—

	TABLE I						
	Total	538	
Delivered elsewhere	21
(1) Placenta prævia	140
(2) Accidental antepartum hæmorrhage	73
(3) Antepartum hæmorrhage of uncertain origin	285
(4) Antepartum hæmorrhage from extraplacental lesions	19

No case is accepted as one of placenta prævia unless the placenta is either felt from below with a finger passed through the cervix or is found to be in the lower segment at abdominal section. The appearance of the placenta after delivery and the clinical features of the case are not accepted as evidence of placenta prævia.

Similarly, no case is defined as accidental antepartum hæmorrhage unless the absence of the placenta from the lower segment is confirmed either by thorough digital exploration from below or at abdominal section. The occurrence of concealed hæmorrhage, while denoting in most cases that the placenta is in the upper segment is not in itself diagnostic since concealed hæmorrhage may occur in placenta prævia.

The adoption of this strict classification has meant that more than half of our cases fall into the group of antepartum hæmorrhage of uncertain origin, and the adoption of a more expectant attitude to cases of antepartum hæmorrhage has led to an increased proportion of cases in this group.

Lesions of the cervix and vagina are diagnosed at the routine examination with a speculum, which is performed when the patient is admitted. It must be emphasized that the presence of, say, a vascular erosion of the cervix does not necessarily exclude a more grave cause for the hæmorrhage.

Four cases of abortion, three of placenta prævia and one of concealed hæmorrhage occurring at the 22nd week are included.

The general maternal mortality for the whole series was 2.7% and the uncorrected foetal mortality was 36.9%.

In the 140 cases of placenta prævia, the maternal mortality was 2.9% and the foetal mortality 52.2%. More detailed analysis shews that out of the 71 infants lost, 38 were lost following the bringing down of a leg to check hæmorrhage. The majority of these cases occurred early in the series and the method has largely been abandoned in recent years.

For the classification of cases of placenta prævia we have used that originally suggested in 1929 by Mr. Norman White. This divides cases of placenta prævia in accordance with the situation of the placenta into four types or degrees. It is suggested that this classification should be universally adopted. It is interesting to note that, so far, the best results have been obtained in cases of fourth degree placenta prævia, largely due to the high incidence of Cæsarean section in the treatment of these cases.

Four mothers lost their lives as a result of placenta prævia, one died from hæmorrhage and shock following a bougie induction and placenta prævia was not diagnosed until autopsy. One died of pulmonary embolism on the seventeenth day after Cæsarean section. The third patient died of shock and hæmorrhage after treatment with Willett's forceps. The fourth patient died of septicæmia due to uterine infection with *Clostridium welchii*. This followed treatment with Willett's forceps and the occurrence of this case and a second similar one where the patient recovered has led to the abandonment of Willett's forceps for the treatment of placenta prævia.

Analysis of the causes of foetal death reveals two main causes—prematurity and placenta separation causing antepartum or intrapartum asphyxia. Cerebral hæmorrhage was found in some cases.

In order to improve the results to mother and infant, certain general principles can be laid down. The first is avoidance of sepsis and the second, preparations to combat hæmorrhage. This means that such cases should never be dealt with outside a properly equipped institution and that a patient suffering from antepartum hæmorrhage should be transferred to hospital at once without any vaginal examination being made.

Once the patient has been admitted, she should be treated expectantly. A speculum is passed and preparations are made for transfusion, but no vaginal examination is made

of their infants was 6 lb. 7 oz. The mothers of the remaining 16 surviving infants, however, had had an average of 1.5 recurrent hæmorrhages during an average period of expectancy of 25.5 days; the average weight of their infants was 5 lb. 15 oz.

In the light of experience acquired in expectant treatment the stillbirths and neonatal deaths of the *whole series* had been reviewed. In the case of 4 stillborn infants and 7 who died their mothers might have been treated expectantly instead of actively on admission. In the case of a further 3 in each of these classes their mothers ought to have been treated expectantly.

Mr. Purdie thanked his colleagues, Mr. K. A. K. Hudson and Mr. D. Friedlander, who allowed him to include cases treated by them.

Comment (A. W. P.).—In any attempt to reduce the maternal and foetal death-rate from placenta prævia the training of the midwife is of great importance. The doctor is criticized if he makes a vaginal examination before sending the patient into hospital. Yet the textbooks for midwives and pupil-midwives still advocate the rupture of membranes by midwives in certain circumstances. Moreover at the examinations conducted by the Central Midwives Board candidates are still expected, by some examiners, to say that they would rupture the membranes themselves. Is it not time that this teaching was altered?

Mr. Rufus C. Thomas supported Mr. Macafee's contention that placenta prævia was not an obstetrical condition which must necessarily be dealt with at the first hæmorrhage. He had adopted this attitude since 1937, during which time 182 cases had been treated. Many of them had been kept in hospital from two to ten weeks before being finally dealt with. The influence of such delay on the chances of survival of the foetus was shown by the fact that of the 182 cases, 125 were dealt with after the 38th week, and a further 25 cases between the 36th and 38th week. The foetal mortality for the whole series was 23%. Two mothers were lost, but neither died from hæmorrhage. One died of pulmonary embolism on the 11th day after Cæsarean section. The other was a case of eclampsia with central placenta prævia, who died in coma shortly after Cæsarean section.

Methods of treatment were on the same lines as those outlined by Mr. Macafee. During the period of expectancy, patients were blood-grouped, hæmoglobin estimations done, and transfusions carried out if necessary. Apart from routine inspection of the cervix, nothing further was done, unless hæmorrhage forced the issue, until the time came for the full examination under anaesthesia. This was carried out in the theatre, with all preparations for the Cæsarean section which might be found necessary. Each patient was assessed for treatment individually.

Willett's forceps were used in 9 cases, and vulsellum forceps in 38 cases, with an infant mortality of 12.8%. No weight was attached to the forceps, traction being only applied if bleeding occurred, and this was released when the bleeding was controlled. It was thought that this intermittent pressure on the placenta enhanced the chances of the foetus. Cæsarean section had been performed in 63 cases.

Internal podalic version had only been used in cases of prolapse of the arm or transverse lie. The mortality had been 100%. 7 cases had been delivered by the breech, this being the presentation on admission. The foetal mortality was 57%, and it was suggested that Cæsarean section should be done in such cases, especially in primigravidae, as the foetal mortality in breech deliveries was so high.

Mr. J. Stallworthy reported 119 consecutive cases of placenta prævia treated at the Radcliffe Infirmary, Oxford, without a maternal death. He welcomed Mr. Macafee's suggestion that the old classification of placenta prævia be scrapped but he advocated that in a case of antepartum hæmorrhage much greater importance should be given to the position of the baby than to the position of the placenta. He felt this was a reform in obstetrical teaching and practice long overdue. He emphasized the importance of the placenta situated posteriorly in the lower uterine segment and illustrated this by a black-board sketch to show how in such cases the true conjugate was shortened by the width of placenta lying over the promontory. This position of placenta was not uncommon and in his series of cases in 31 treated by Cæsarean section 14 had this type of placenta. Unless its importance was recognized it was most dangerous as it so often arrested descent of the presenting part and by making hæmorrhage difficult to control placed both mother and infant in grave danger. In his opinion this type of case with the head above the brim should be treated by Cæsarean section.

The President said it was evident from the figures presented by Mr. Macafee that if the foetus was alive and viable one of two methods of active treatment of placenta prævia should be adopted, i.e. rupture of membranes or Cæsarean section. Podalic version

graduate Medical School, Hammersmith Hospital. In 108 cases of placenta prævia the foetal mortality was 19·4%; 33 had been treated expectantly with a foetal mortality of 9%. During the first six years the total infant mortality (stillbirths and neonatal) was 29·2%, but with increasing resort to expectancy in the last five years this had been reduced to 13·4%. In 77 booked cases the infant mortality was for the whole period 13%.

Professor Young pointed out that, where the antepartum bleeding was due to accidental hæmorrhage, expectant treatment had not reduced the infant loss. In a total of 162 cases the infant mortality was 32·7%. Of these 43 had been treated expectantly with a combined stillbirth and neonatal mortality rate of 30·2%.

Professor Munro Kerr: I am in the unique position of being able to recollect the ridicule that was hurled against Lawson Tait in the late eighties of the last century, when he proposed Cæsarean section for placenta prævia. The pendulum has made its full swing. The question today is not under what circumstances Cæsarean section should be performed for placenta prævia, but rather under what circumstances the operation of Cæsarean section should *not* be performed for this complication.

It would appear that there remain really only two methods of treatment for placenta prævia, provided the patient is in an institution and has not to be treated in unfavourable surroundings, when of course the best in the circumstances must be done, which is probably podalic version and bringing down a foot for the graver forms of the complication.

The alternatives are rupture of the membranes for the slighter cases of lateral placenta prævia and Cæsarean section for all others. But even if rupture of the membranes is performed in this limited group, the foetal mortality rate is something like 15% to 20%, and with little prospect of reducing it.

Most important is the matter that has been stressed by several speakers and particularly by Mr. Macafee that everything must be done to carry on the pregnancy to as near term as possible, in order to reduce the foetal mortality from prematurity to its lowest limits. Then, when the child has reached anything over the 36th week, Cæsarean section will undoubtedly save the greatest number of infants, without unduly risking the mother's life.

Professor Munro Kerr was very hopeful that by some means it would be possible to improve the technique for localizing the position of the placenta by radiography. It would be of enormous advantage in cases of uterine hæmorrhage in the later months, if the exact position of the placenta could be located.

Mr. A. W. Purdie said that in the maternity department of the North Middlesex County Hospital during the years 1940 to 1944 inclusive there had been 143 cases of placenta prævia among 6,921 deliveries.

There had been 1 maternal death (0·69%). This occurred in an "emergency" case of lateral placenta prævia (Type I). Cæsarean section had been performed as artificial rupture of the membranes (cervix one fingerbreadth dilated) failed to arrest the hæmorrhage. The uterus had been atonic, never really contracting well. Hæmorrhage recurred at the close of the operation, and she died shortly afterwards in spite of continuation of the blood transfusion and packing the uterus. This death might perhaps have been avoided if, before closing the abdomen, hysterectomy had been performed.

Of 147 infants born, 100 (68·03%) remained alive, 20 (13·60%) were stillborn and 27 (18·36%) died. The combined foetal mortality was 47 (31·97%). No eliminations were made on account of prematurity as this was considered to be due to the maternal placenta prævia.

EXPECTANT TREATMENT

With the more liberal use of blood transfusion and Cæsarean section there had been improvement in recent years in both maternal and foetal results. Further improvement in the latter seemed to lie in expectant treatment of the maternal hæmorrhage—where that was possible without increasing the maternal risk.

Expectant Treatment in this Series

Forty-one cases had been treated expectantly over periods varying from 12 hours to 67 days. The majority of these had been treated, at the end of the waiting period, by artificial rupture of the membranes or Cæsarean section (with or without examination under anaesthesia) or had gone into labour spontaneously and had required no treatment.

No maternal death had occurred in any case treated expectantly.

Of 43 infants born to these mothers 32 (74·4%) had survived finally, 5 (11·6%) were stillborn and 6 (14%) died. The mothers of 16 of the surviving infants had had no recurrent hæmorrhages in an average waiting period of 19·75 days: the average weight

in the glomerulus of the kidney. At the distal end of the capillary the hydrostatic pressure of the blood has been dissipated in friction and, being now below the colloid osmotic pressure of the plasma proteins, is low enough to allow tissue fluid to enter the plasma. If the blood were stationary, exchange of solutes would still take place through the capillary wall, e.g. glucose would still diffuse from plasma to tissue fluid and urea from tissue fluid to plasma, but the actual ebb and flow of fluid, which is a consequence of the mechanical features of the circulation and which must materially assist in metabolic exchange, would be absent.

Factors maintaining an equilibrium between plasma and tissue fluid which are rather more difficult to assess concern the permeability of the capillary wall to protein, and the actual mechanical pressure existing in the tissues. With regard to the first point it is well known that tissue fluid contains a trace of protein and that this may, in some circumstances, increase, and it is questionable whether the permeability of the capillary wall is a constant factor. With regard to the second point, it is clear that filtration through the walls of the capillaries in the general tissues of the body is not strictly comparable to that in the glomerulus of the kidney for two reasons. First, the hydrostatic pressure is lower, and secondly, instead of the filtrate being freely drained away by the tubule, it is being driven into a space which is already "full". There must, therefore, be a mechanical obstruction to filtration should anything occur to lessen the return of tissue fluid to the blood stream either directly or through the lymphatics. It is possible to do little in the way of measuring these two factors, but they must be borne in mind.

It is taken for granted that the osmotic pressure of all the fluid compartments is the same, and it may be assumed for all practical purposes that if the osmotic relations between intracellular and extracellular fluid are disturbed, equalization can be achieved in the first instance only by passage of water through the cell membrane which is impermeable to the majority of ions. The osmotic pressures thereby become equalized at a somewhat abnormal level. Such transfers of fluid may be minimized by purely extracellular adjustments. Thus, if the extracellular fluid became more dilute than the intracellular fluid, the requirements of osmotic equilibrium would result in passage of water into the cells, but this could be rapidly corrected by either excretion of the excess water or retention of sodium chloride by the kidneys. The sodium chloride would be confined to the extracellular fluid, and would enable all the retained water to be accommodated in this compartment without disturbing the osmotic pressure inside the cells. However, the volume of the extracellular compartments would be increased.

In order to estimate the total volume of extracellular fluid, it is necessary to find a substance which is readily diffusible through the capillary endothelium, which will not diffuse into the cells of the body, and which is sufficiently slowly excreted to enable it to become evenly distributed. Sodium thiocyanate fulfils these requirements very closely, and the degree to which a measured amount becomes diluted when introduced into the body furnishes a measure of the volume of the combined extracellular compartments. To obtain the volume of plasma it is necessary to inject into the blood stream a substance which is not diffusible through the capillary endothelium, but whose molecules are not sufficiently large to be attractive to the reticulo-endothelial system. The substance generally used is Evans Blue, and dilution of a given amount enables the plasma volume to be computed. By difference the volume of the interstitial fluid is found.

The state of affairs in pregnancy.—It has long been assumed that water retention takes place in pregnancy, but until methods for the quantitative assessment of body water became available this was not easy to prove. The comparison of intake and output is difficult on both technical and theoretical grounds. Technically, on account of the water associated with every article of diet and on account of the loss of water by evaporation, and theoretically, because of the interconversion of the three main types of food-stuff with consequent variations in metabolic water in a subject whose weight is steadily increasing.

Various balance experiments have been carried out on the inorganic constituents of the diet, and there can be little doubt that a retention of sodium occurs during the latter part of pregnancy and perhaps throughout its course. The findings of five sets of investigators are summarized by Chesley (1944), and they show a gain of from 1.6 to 8.8 grammes of sodium per week. A representative figure would seem to be about 3 grammes. If all this sodium were osmotically active, about a litre of water a week would have to be accommodated in the extracellular compartments in order to maintain the osmotic pressure of the body fluids at a normal level. Although the various researches covered only a few weeks, the inference is inescapable that such a retention

and bringing down a foot, or bringing down a foot if the breech presented, resulted in a foetal mortality that was far too high, and the same was true of Willett's forceps. Artificial rupture of membranes should, however, only be carried out if good contractions were present and the os dilating. He thought that location of the placental site by injecting a radiopaque substance into the amniotic cavity was of little value in diagnosis, for it induced premature labour in about half the cases and could not therefore be used till after the 36th week, and it might even cause intrauterine death of the foetus. In one of his cases its use resulted in a pus-discharging sinus communicating with the amniotic cavity and though the patient recovered it caused considerable anxiety. Most of the cases of antepartum hæmorrhage treated expectantly went into labour spontaneously at term and gave birth to a living child without further bleeding or any interference, and the cause of the hæmorrhage then remained undiagnosed. Such cases appeared in the hospital report as "antepartum hæmorrhage of doubtful origin" and each year formed by far the largest group. In backward countries such as Professor Nixon had described one must do the best one could in the circumstances and no doubt podalic version and extracting a foot might there be a useful measure. The question was sometimes put to him by students: "What is one to do in a case of severe A.P.H. 20 miles from a hospital? Should not the vagina be plugged before moving the patient?" His own experience was that bleeding had always ceased when one got to the house. Plugging the vagina would almost certainly start a fresh hæmorrhage. It was better to give $\frac{1}{2}$ grain of morphia and as soon as the patient had recovered sufficiently from shock to transfer her to hospital without any further interference. He did not think there was any place for the use of the vaginal plug in the hospital or outside.

In reply to the President, Mr. Phillips stated that the methods he used, including plugging, were the result of an attempt to try to obtain good results as far as the mother was concerned, more or less ignoring the foetus, and by using obstetric methods rather than Cæsarean section.

Only 10% of the cases were treated by Cæsarean section, yet the maternal mortality rate was only 1.4%. He thought that there was still a use for vaginal plugging, though a much less frequent use than in the past. He also thought that by increasing the number of Cæsarean sections, a much lower foetal mortality rate would be obtained.

[January 18, 1946]

DISCUSSION ON BACTERIÆMIA IN PUERPERAL SEPSIS

Openers: Mr. James Wyatt, Dr. R. Cruickshank and Dr. A. M. Ramsay.

There was a lengthy discussion in which many other speakers took part (see *Brit. med. J.*, 1946 (i) 175; *Lancet*, 1946 (i) 163).

[February 15, 1946]

DISCUSSION ON WATER METABOLISM IN PREGNANCY

Professor W. H. Newton: *The water compartments of the body.*—The water of the body is now conventionally divided into three compartments—intracellular water, interstitial or tissue fluid, and blood plasma. The ions (for instance, potassium and phosphate) which predominate in solution in the intracellular water are so different from those (for instance, sodium and chloride) which are common to the interstitial fluid and blood plasma, that the cell membrane is clearly the most important barrier. The fluid in the last two compartments is so similar that they may be regarded as sub-divisions of a single larger compartment, the extracellular fluid. The extracellular fluid may be looked upon as the *milieu interne* of Claude Bernard, and the circulation of the blood as a means of stirring it. Since the walls of the capillary blood-vessels are thought to be permeable to all constituents of the blood plasma with the exception of the plasma proteins, it follows that if the plasma proteins were absent the circulatory system could scarcely be regarded as closed, and an effective circulation would be difficult if not impossible to maintain. The function of the plasma proteins is, in virtue of their osmotic pressure, to hold a certain amount of fluid together with its solutes within the circulatory channels. According to the well-known theory of Starling, the mechanical pressure whose primary object is to circulate the blood is still, at the proximal end of the capillary, greater than the osmotic pressure of the plasma protein, and is able to drive a protein-free filtrate through the capillary walls in much the same way as occurs

in the glomerulus of the kidney. At the distal end of the capillary the hydrostatic pressure of the blood has been dissipated in friction and, being now below the colloid osmotic pressure of the plasma proteins, is low enough to allow tissue fluid to enter the plasma. If the blood were stationary, exchange of solutes would still take place through the capillary wall, e.g. glucose would still diffuse from plasma to tissue fluid and urea from tissue fluid to plasma, but the actual ebb and flow of fluid, which is a consequence of the mechanical features of the circulation and which must materially assist in metabolic exchange, would be absent.

Factors maintaining an equilibrium between plasma and tissue fluid which are rather more difficult to assess concern the permeability of the capillary wall to protein, and the actual mechanical pressure existing in the tissues. With regard to the first point it is well known that tissue fluid contains a trace of protein and that this may, in some circumstances, increase, and it is questionable whether the permeability of the capillary wall is a constant factor. With regard to the second point, it is clear that filtration through the walls of the capillaries in the general tissues of the body is not strictly comparable to that in the glomerulus of the kidney for two reasons. First, the hydrostatic pressure is lower, and secondly, instead of the filtrate being freely drained away by the tubule, it is being driven into a space which is already "full". There must, therefore, be a mechanical obstruction to filtration should anything occur to lessen the return of tissue fluid to the blood stream either directly or through the lymphatics. It is possible to do little in the way of measuring these two factors, but they must be borne in mind.

It is taken for granted that the osmotic pressure of all the fluid compartments is the same, and it may be assumed for all practical purposes that if the osmotic relations between intracellular and extracellular fluid are disturbed, equalization can be achieved in the first instance only by passage of water through the cell membrane which is impermeable to the majority of ions. The osmotic pressures thereby become equalized at a somewhat abnormal level. Such transfers of fluid may be minimized by purely extracellular adjustments. Thus, if the extracellular fluid became more dilute than the intracellular fluid, the requirements of osmotic equilibrium would result in passage of water into the cells, but this could be rapidly corrected by either excretion of the excess water or retention of sodium chloride by the kidneys. The sodium chloride would be confined to the extracellular fluid, and would enable all the retained water to be accommodated in this compartment without disturbing the osmotic pressure inside the cells. However, the volume of the extracellular compartments would be increased.

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Various balance experiments have been carried out on the inorganic constituents of the diet, and there can be little doubt that a retention of sodium occurs during the latter part of pregnancy and perhaps throughout its course. The findings of five sets of investigators are summarized by Chesley (1944), and they show a gain of from 1.6 to 8.8 grammes of sodium per week. A representative figure would seem to be about 3 grammes. If all this sodium were osmotically active, about a litre of water a week would have to be accommodated in the extracellular compartments in order to maintain the osmotic pressure of the body fluids at a normal level. Although the various researches covered only a few weeks, the inference is inescapable that such a retention

would more than account for the average observed gain in weight during pregnancy. So far as it is possible to draw conclusions from average figures obtained by different observers under different conditions, it would appear that the sodium is not all osmotically active. Nevertheless, it is reasonable to suppose that some of it is, and Thompson and Pommerenke (1939) have shown that fluctuations in the sodium and chloride balances are parallel. Moreover, Freyberg, Reekie and Folsome (1938) showed that the administration of sodium chloride for a few days during pregnancy was accompanied by an increase of body-weight, and that on withdrawing sodium chloride the weight was again reduced. Their estimations of water balance showed clearly that the variations in body-weight were due to retention and excretion of water. Their calculations of total water exchange in one subject during the last three months of pregnancy indicated a retention of only 600 grammes, but their patient had the lowest of the positive sodium balances recorded by Chesley in his review.

If salt and water retention are related in the way we have suggested we should expect to find an increase in the plasma volume and in the interstitial fluid during pregnancy, and these have actually been established. The increase in plasma volume has been confirmed by too many observers to quote (*see* Dieckmann & Wegner, 1934), but recent investigators are Mull and Bill (1945) and Albers (1939). The increases are between 20 and 30%. Chesley (1943) found the total gain of extracellular water during pregnancy to average 6.3 litre, of which 1.5 to 2 litres were probably in the products of conception, 0.7 litre in the new tissue of the uterus and breasts, and 1.3 litres in the blood plasma. This leaves about 2.5 litres (5.5 pounds) as the share of the extra-genital interstitial fluid. Since the volume of the interstitial or tissue fluid of the normal individual is probably more than four times the volume of the plasma this estimate of Chesley's is lower than we should expect, even if the uterus and breasts are included, and it is natural to look for further factors leading to selective retention of water in the plasma. Instead, we find factors operating in the reverse direction. The first of these is a drop which may be as much as 20% in the colloid osmotic pressure of the plasma due to a diminution in the concentration of plasma proteins. It is to be presumed that an additional volume of water in the extracellular fluid would be divided between its two compartments in the ratio of their original volumes, only if the conditions determining the ratio remained unaltered. The chief condition, as we have seen, is the concentration of plasma proteins, and its diminution should lead to the interstitial fluid compartment receiving rather more than its share of the excess water. In pregnancy with oedema, according to Albers, the plasma protein is yet further reduced and an increase in the protein content of the tissue fluid makes the effective colloid osmotic pressure of the plasma still lower.

Another factor is the increase in the venous pressure in the legs which has been convincingly demonstrated by McLennan (1943). He followed the pressure in the femoral vein throughout pregnancy by measurements in 255 women. The measurements were made by entering the vein and reading the pressure directly from a manometer with the subjects recumbent. The average rise was from 9 cm. of water in early pregnancy to about 24 cm. at term. This rise, which does not take place in the antecubital vein, may be due either to external pressure on the great veins within the abdomen, or to a large inflow from the uterine veins having the effect of obstructing the inflow from the legs. As the legs constitute 37% of the body-weight, the consequent increase in filtration pressure in the capillaries must drive an appreciable amount of fluid from the plasma into the interstitial fluid compartment. This might, however, be limited by an increase of pressure within the tissues themselves. Investigations of a third factor in normal pregnancy—the permeability of the capillary walls—yield results which tend to be unconvincing, but no one has yet alleged that the permeability is diminished.

We are, therefore, faced with the situation that an increase in water content of the plasma and interstitial fluid during pregnancy has been demonstrated, but that the distribution of the fluid between these two compartments is not fully accounted for. It will be noticed that the relation between the total 6.3 litres of extracellular fluid and the 1.3 litres attributed to blood plasma is not unlike that obtaining between the normal extracellular fluid and plasma volumes. There may be a fallacy in Chesley's assumption that so much of the thiocyanate-available water is in the products of conception, or pregnancy may introduce an error into the method of estimating blood volume. Added to these difficulties is the fact that evidence of an increase in the water content of any isolated organ or tissue in pregnant animals is lacking.

In an attempt to account for the retention of sodium and water during pregnancy, Taylor, Warner & Welsh (1943) administered oestrogens and progesterone to

their subjects and achieved some success in showing that this, in fact, led to such retention. It is certainly true, as they point out, that the pregnant woman is exposed to the action of these hormones in large quantities during pregnancy, and they are known from the work of Zuckerman, Palmer and Bourne (1939) and others to cause accumulation of water in certain situations in monkeys.

The weight changes of pregnancy are of great interest but not very helpful in this connexion. It seems certain that most animals increase the weight of their own extra-genital tissues during pregnancy, and Van Wagenen and Newton (1943) have shown that after removal of the foetus, provided the placenta is left attached to the uterus, the macaque monkey may resume its normal gain in weight until it delivers the placenta at term. There can be little doubt, however, from a study of Chesley's review, that if average figures are to be used as a basis for computation, either the nitrogen (if built into protoplasm) or the sodium (if osmotically active) which are retained during human pregnancy would be sufficient to account for the gain in weight. It must be admitted that the quantitative balance sheet of the various maternal gains during pregnancy leaves much to be desired, and that average figures are not a very satisfactory foundation on which to build.

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Mr. G. W. Theobald: A man may live for over six weeks without food, but deprive him of water and he will die within from twenty-four hours to just over a week, depending on the temperature and humidity of his environment, and the amount of work he does. Every active cell of the human body is bathed by the interstitial fluid from which it derives its nourishment and into which it discharges its waste products of metabolism. This fluid, moreover, forms the reservoir on which the body draws for considerable supplies with which to fashion the gastric, pancreatic and other juices and secretions of the body, the sweat necessary for the regulation of its temperature, and the solvent for the waste products excreted through the kidneys.

The amount of this fluid varies within considerable limits. If water is withheld this supply is first drawn upon before the cells and blood plasma are required to part with their water. Nevertheless the red blood cell count may exceed 6 million per cubic millimetre before serious symptoms occur (Allison and Critchley, 1943). On the other hand an excess of fluid in the tissues may cause cerebral convulsions or acute oedema of the lungs. It must therefore be conceded that the control of the water balance of the body is the most important function subserved by the kidneys.

Every active cell in the body is freely permeable to water, but in no case do its organic salts bear any relation to those of its environment. It is thus evident that the higher forms of life are dependent on the selective permeability of the membranes of the cells of which they are composed. The heart pumps some 5 litres of blood through the arteries every minute, so that the speed of the circulation must be very considerable. It is therefore proper and important to regard the interstitial fluid as a constantly agitated fluid which is frequently changed.

It is generally assumed that the average man drinks some 1,500 c.c. of water and absorbs a further 800 c.c. with his food each day. Oxidative processes result in the formation of about 300 c.c. during the same period of time. He excretes approximately 1,500 c.c. as urine, 600 c.c. through his skin, 400 c.c. through his lungs, and 100 c.c. in his faeces. During exercise in hot weather several litres of water may be lost through the skin, and similar amounts may be passed through the bowel during an attack of diarrhoea. The body must provide this water but neither the skin, nor the lungs, nor the bowel can be considered in any way responsible for regulating the water balance of the body.

The body's need for water is signalled by the sensation of thirst which in extreme cases has been described as "the devouring fire of thirst, of all human wants the most insupportable and the most pressing".¹ This has been thought to be normally

¹Narrative of the loss of the *Fattysalam*, quoted by Allison and Macdonald Critchley.

would more than account for the average observed gain in weight during pregnancy. So far as it is possible to draw conclusions from average figures obtained by different observers under different conditions, it would appear that the sodium is not all osmotically active. Nevertheless, it is reasonable to suppose that some of it is, and Thompson and Pommerenke (1939) have shown that fluctuations in the sodium and chloride balances are parallel. Moreover, Freyberg, Reekie and Folsome (1938) showed that the administration of sodium chloride for a few days during pregnancy was accompanied by an increase of body-weight, and that on withdrawing sodium chloride the weight was again reduced. Their estimations of water balance showed clearly that the variations in body-weight were due to retention and excretion of water. Their calculations of total water exchange in one subject during the last three months of pregnancy indicated a retention of only 600 grammes, but their patient had the lowest of the positive sodium balances recorded by Chesley in his review.

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be true it is evident that the hydræmic state lessens the number of red blood corpuscles lost during delivery and favours an easy return to the normal blood count when the vascular bed once again returns to its former size.

On the other hand the dilution of the blood lowers the effective osmotic pressure of the plasma colloids and thereby facilitates the escape of fluid from the capillaries to the tissue spaces. This increased loss of fluid from the arterial end of the capillary will clearly cause a correspondingly enhanced concentration of the plasma colloids at the other end of the capillary, and consequently prevent any progressive loss of fluid to the tissues. It is of course important to make sure that the woman's intake of first class proteins is adequate throughout the course of pregnancy, otherwise the effective osmotic pressure of the plasma colloids will fall still further.

The storage of sodium.—It is believed that the increase in the amounts of the sex steroids circulating in the blood is responsible for the storage of nitrogen, sodium and other substances during pregnancy. Heilig (1924) was the first to call attention to a disturbance in the water metabolism at the time of menstruation. Thorn, Nelson and Thorn (1938) found that œstrone, progesterone, pregnandiol and testosterone induced retention of sodium chloride and water in normal dogs. They further reported that sodium chloride and water were retained during both the intra- and the pre-menstrual phase of the cycle in man, and that the onset of menstruation was associated with an increased renal excretion of these substances.

If these facts be accepted the difficulty to be faced is not whether the stored sodium could cause water retention but why every pregnant woman does not drown in her own interstitial fluid. The estimates of the amounts of sodium retained during pregnancy vary from 0.23 to 1.26 grammes *daily*. If it be assumed that this sodium is osmotically active and is held extracellularly it would involve the retention of from 500 to 2,600 c.c. of water *each day*. Further Hummel *et alia* (1936) found that a nursing mother retained 22 to 27 grammes of sodium in a period of forty-three days. We know, moreover, that the postpartum diuresis occurs while the blood is still hydræmic, and while the excess sodium is still in the tissues. It may therefore be asserted with confidence that neither of these factors, nor both of them acting in concert can be the sole or even the determining factor in causing water retention during pregnancy. The sodium must be stored for the most part in an osmotically inactive form in the tissues.

The increase in weight during the course of pregnancy.—Chesley (1944) concludes from the study of several reports that the average total gain during normal pregnancy is 24 lb., with a standard deviation of 45%, or 10.8 lb. Applying this standard to the pooled data he collected from the literature he concluded that two-thirds of all normal patients may be expected to gain between 13 and 35 lb. during the course of pregnancy, and that about one-sixth of all normal patients may be expected to gain more than 35 lb. McIlroy and Rodway (1937) reported that the maximal gain occurred between the 24th and 28th weeks, and many observers aver that a loss of weight may occur during the last two weeks of pregnancy.

Estimates of the amount of nitrogen stored during pregnancy are as high as 1 lb., which would represent more than 6 lb. of protein. If this protein were used in the formation of new tissue it would involve an increase in weight of no less than 30 lb. It may consequently be assumed that the nitrogen, like the sodium, is stored as such, possibly in the liver.

The following figures may be taken as substantially correct and account for most of the increase in weight during pregnancy.

	lb.
(1) The products of conception	11.5
(2) The uterus and adnexa	2.5
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occasioned by a diminution of the salivary secretion, which may be relieved by the injection of pilocarpine, and occasioned by an injection of atropine. The sensation of thirst has, however, been reported in association with excessive salivation (Allison and Critchley, 1943). It must be regarded as a somewhat crude criterion of the degree of hydration of the tissues, and there is often a measurable time lag between the sensation of thirst and a relative degree of dehydration of the tissues. In animal experiments it is not infrequently observed that the dog's tissues are relatively dehydrated although the animal had free access to water. Conversely the animal may drink water greedily immediately it is returned to its cage, shortly after the administration of 250 c.c. of water through the stomach tube.

The small intestine demonstrates a remarkable avidity for water, and absorbs whatever is offered. It was a common custom for German students when *auf die Kniepe* to challenge a companion to drink up to 30 pints of beer within a short period of time. None of this beer was voided through the bowel, it all escaped through the kidneys. What happens to the water after it is absorbed? Klisiecki, Pickford, Rothchild and Verney (1933) concluded, both from their own experiments and from those reported by others, that 250 c.c. of water are absorbed from the small gut of a dog weighing 10 kg. within a period of 36 minutes, that is to say a full 15 minutes before the peak of water diuresis occurs. Further, the peak of water diuresis does not occur until the water load curve has fallen to 76% of its maximum. The water is indubitably absorbed into the blood stream, is offered to the kidneys and refused, and is consequently deposited in the tissue spaces. It does not stay in the blood, for however great be the quantity of water imbibed relatively little dilution of the blood is thereby occasioned.

It is thus clear that the kidneys, the watchdogs of the water exchequer of the body, take from 15 to 30 minutes to make up their minds to open the sluices and let the excess water from the tissues escape. Each human kidney is believed to contain $4\frac{1}{2}$ million glomerulo-tubular units. Assuming that 1 c.mm. of filtrate passed through each glomerulus in an hour, a rate which is known to obtain in the frog, 900 c.c. of urine would be secreted each hour even if 90% of the filtrate were reabsorbed by the tubules. This fact, taken in conjunction with others, led to the view which has been discarded by many modern workers, that the glomerulo-tubular units do not all function at the same time, but enjoy rest pauses. The structure of the kidney certainly makes it possible for blood entering the kidneys to pass direct from the vasa recta into the interlobular capillaries, and thus to by-pass the glomeruli. So far as I am aware the maximum rate of urinary secretion attained by man is in the neighbourhood of 1,200 c.c. an hour, a rate which cannot be long maintained.

Although nervous impulses normally affect the amount of blood supplied to the kidneys, it is beyond dispute that free water diuresis can occur after both kidneys have been completely denervated. The most fascinating and most satisfactory solution of this problem so far advanced, is that minute quantities of the post-pituitary anti-diuretic substance circulating in the blood, cause the tubules to reabsorb most of the water from the glomerular filtrate. It is only when the inhibition occasioned by this substance is temporarily withdrawn that water diuresis can occur.

What are the factors associated with pregnancy which may disturb the normal regulation of the water balance of the body? I shall not discuss the aetiology of the pregnancy toxæmia and their possible association with water retention. The relevant known facts are: (1) A state of hydræmia obtains during pregnancy and is associated with an increase of the blood volume by approximately 20%. (2) The pregnant woman is known to store nitrogen, sodium, iron and other substances. (3) The woman increases in weight during the course of pregnancy. (4) The weight and bulk of the gravid uterus occasion certain mechanical disadvantages which tend to increase until the 38th week of pregnancy.

The increase in the blood volume.—The simplest and most satisfactory explanation of this phenomenon is that it is necessitated by the rapid increase in the size of the vascular bed. The increase of the blood volume results in a compensatory hydræmia. We know that in some forms of anaemia the vascular bed may shrink to approximately half of its normal size, and this device undoubtedly represents nature's effort to make the most of such blood cells as are available, the direct opposite of the course which must be pursued during pregnancy. It would, indeed, be difficult to envisage any other method open to nature to deal with this plumbing emergency.

The hydræmia of pregnancy possibly offers certain advantages. It has been suggested, for example, that the consequent lowering of the blood viscosity facilitates the exchange of oxygen and nourishment through the placental membranes. Whether or not this

be true it is evident that the hydræmic state lessens the number of red blood corpuscles lost during delivery and favours an easy return to the normal blood count when the vascular bed once again returns to its former size.

On the other hand the dilution of the blood lowers the effective osmotic pressure of the plasma colloids and thereby facilitates the escape of fluid from the capillaries to the tissue spaces. This increased loss of fluid from the arterial end of the capillary will clearly cause a correspondingly enhanced concentration of the plasma colloids at the other end of the capillary, and consequently prevent any progressive loss of fluid to the tissues. It is of course important to make sure that the woman's intake of first class proteins is adequate throughout the course of pregnancy, otherwise the effective osmotic pressure of the plasma colloids will fall still further.

The storage of sodium.—It is believed that the increase in the amounts of the sex steroids circulating in the blood is responsible for the storage of nitrogen, sodium and other substances during pregnancy. Heilig (1924) was the first to call attention to a disturbance in the water metabolism at the time of menstruation. Thorn, Nelson and Thorn (1938) found that *œstrone*, progesterone, pregnandiol and testosterone induced retention of sodium chloride and water in normal dogs. They further reported that sodium chloride and water were retained during both the intra- and the pre-menstrual phase of the cycle in man, and that the onset of menstruation was associated with an increased renal excretion of these substances.

If these facts be accepted the difficulty to be faced is not whether the stored sodium could cause water retention but why every pregnant woman does not drown in her own interstitial fluid. The estimates of the amounts of sodium retained during pregnancy vary from 0.23 to 1.26 grammes daily. If it be assumed that this sodium is osmotically active and is held extracellularly it would involve the retention of from 500 to 2,600 c.c. of water each day. Further Hummel *et alia* (1936) found that a nursing mother retained 22 to 27 grammes of sodium in a period of forty-three days. We know, moreover, that the postpartum diuresis occurs while the blood is still hydræmic, and while the excess sodium is still in the tissues. It may therefore be asserted with confidence that neither of these factors, nor both of them acting in concert can be the sole or even the determining factor in causing water retention during pregnancy. The sodium must be stored for the most part in an osmotically inactive form in the tissues.

The increase in weight during the course of pregnancy.—Chesley (1944) concludes from the study of several reports that the average total gain during normal pregnancy is 24 lb., with a standard deviation of 45%, or 10.8 lb. Applying this standard to the pooled data he collected from the literature he concluded that two-thirds of all normal patients may be expected to gain between 13 and 35 lb. during the course of pregnancy, and that about one-sixth of all normal patients may be expected to gain more than 35 lb. McIlroy and Rodway (1937) reported that the maximal gain occurred between the 24th and 28th weeks, and many observers aver that a loss of weight may occur during the last two weeks of pregnancy.

Estimates of the amount of nitrogen stored during pregnancy are as high as 1 lb., which would represent more than 6 lb. of protein. If this protein were used in the formation of new tissue it would involve an increase in weight of no less than 30 lb. It may consequently be assumed that the nitrogen, like the sodium, is stored as such, possibly in the liver.

The following figures may be taken as substantially correct and account for most of the increase in weight during pregnancy.

	lb.
(1) The products of conception	11.5
(2) The uterus and adnexa	2.5
(3) Breasts	3.0 ± 1
(4) Increase in the blood volume	2.5
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during pregnancy. The legs, arms and face almost invariably increase in size during the course of pregnancy, and a shrinkage in all these three areas is noticeable after delivery and can be correlated with a post-partum water diuresis. The wedding ring must be loose indeed if it does not become tight during pregnancy.

If it may be assumed that an excess of not more than one litre of water may be held in the tissues during the course of normal pregnancy, what would be the maximum amount of water that could be held before visible signs of œdema occurred? I have drunk two litres of water within twenty minutes and this was followed by an unpleasant occipital headache which lasted for several hours, and curiously enough by a metallic taste in the mouth which lasted for more than forty-eight hours. I know of no figures, but should be disposed to doubt whether any woman could hold more than three litres of excess fluid in her tissue spaces without experiencing unpleasant symptoms, and manifesting œdema. These additional two litres would not weigh as much as 5 lb.

Weight gain in relation to the pregnancy toxæmias.—It seems to be an established fact that an abnormal gain in weight frequently precedes the manifestation of toxæmic symptoms. McIlroy and Rodway reported that their 75 toxæmic patients showed a 50% greater increase of weight between the 24th and 38th weeks of pregnancy than their normal patients. Siddall and Mack (1938) found that 61% of their 100 toxæmic patients showed weight gains of at least twice the average at one or more periods after the seventh lunar month, but that the other 39% "had no excessive gain at any time". Indeed, these women gained an average of only 11·6 lb. as compared with 15·7 lb. in normal patients. They also found that 45% of their normal patients showed relatively excessive gains of weight at one or more periods during the last four months of pregnancy.

There has been much confusion of thought with regard to the significance of weight increases in pregnancy. It is beyond dispute that apparently normal women may gain more than 35 lb. during the course of pregnancy. If the weighing of expectant mothers be carried out with a view to detecting the incipient pregnancy toxæmias, and it be assumed that water retention is the incriminating factor, then an increase in weight not exceeding 5 lb. is all that can be anticipated. It follows that a *sudden increase* in weight during the last few weeks of pregnancy may be caused by water retention and be significant. Most available figures suggest that in more than 50% of cases these gains, be they never so sudden, are without significance. The regular weighing of expectant mothers is very important, but provides evidence which is suggestive rather than conclusive.

When does water retention proceed to frank œdema?—œdema can only occur, whether during pregnancy or at any other time, when the permeability of the capillaries is altered either by: (1) malnutrition, (2) chemical poisons or (3) physical injury. Malnutrition may be occasioned by local congestion or represent a local manifestation of the effects of inadequate nutrition. Cohnheim (1909) showed that after long-continued anæmia of the rabbit's ear, the vessels became so permeable that the restoration of the normal circulation was followed by marked œdema of all the tissues. He also found that ligation of the femoral vein in the dog did not cause œdema in a healthy dog, but did if the animal were first rendered anæmic by frequent bleeding. Dr. McMichael authorizes me to say that he has found that if an armlet be applied to the arm of a normal individual, and the pressure in it be raised to 60 mm.Hg, only a limited amount of swelling of the arm will occur below the constriction. The same procedure carried out on a patient suffering from heart failure will result in marked œdema formation. The effects of general malnutrition on the permeability of the capillaries are well exemplified in ankylostomiasis and the wet form of beri-beri. The effects of stagnation on their permeability is evident in cases of heart failure.

The operation of mechanical factors during the course of pregnancy.—I have shown elsewhere (Theobald 1932, 1933) that the bulk of the gravid uterus is liable to elevate and cause a relative fixation of the diaphragm, and thus to raise the intra-thoracic pressure and indirectly increase the general intravenous pressure throughout the body. The weight and bulk of the pregnant uterus cause a more direct and more marked increase of pressure in the veins draining the lower extremities and the lower abdomen, so long as the woman adopts the sitting or the standing position.

Water diuresis (Theobald 1934) curves obtained from normal pregnant women show that they are usually incapable of attaining much more than half the normal rate of urine secretion, neither can they void more than approximately half the amount of water within two and a half hours of its being drunk, so long as they remain either sitting or standing. The intravenous injection of 0·01 unit of post-pituitary extract

nevertheless inhibits water diuresis in these patients, and this fact strongly suggests that the kidneys are willing to excrete the water which is offered to them. It is reasonable to assume that the inadequate water diuresis results from the fact that the water is held in the tissues and is not presented to the kidneys for excretion.

Striking support for this contention is obtained by a very simple experiment (Theobald and Verney, 1935). A normal individual should pass a litre of urine within two and a half hours of drinking that amount of water, and he should reach the peak of diuresis in from 50 to 60 minutes. If he stands absolutely still in the upright position he will not excrete even half the amount of water he imbibes. The probable explanation for this fact is that the absence of muscular contractions in the legs allows the blood to stagnate in the veins, and the water to escape into the tissues. Support for this conjecture is obtained by the simple expedient of bandaging the legs and thighs firmly before the upright position is adopted. The individual will then pass more than 600 c.c. of urine within two and a half hours.

CONCLUSIONS

If we are justified in assuming that an excess of water not exceeding 1 litre may be retained in the tissues during normal pregnancy, and that an additional 2 litres in the tissue spaces is the extreme limit that can be held without causing obvious signs and symptoms, then the additional weight of water in the tissues which precedes the onset of toxæmic symptoms cannot be greater than 5 lb. It is therefore only a sudden, and relatively small increase in weight between the 28th and 38th weeks of pregnancy that can be of suggestive significance.

At least four factors have been regarded as responsible, either in part or in whole, for the excessive water retention which may occur during pregnancy, and they are: (1) The hydræmic state of the blood, and the consequently lowered osmotic pressure of the colloids of the blood plasma, (2) The retention of sodium, (3) The excessive amounts of the sex steroids circulating in the blood, and (4) The mechanical disadvantages occasioned by the size and weight of the gravid uterus. I would stress that *all* of these factors *always* operate during the course of pregnancy, and yet at least 90% of all expectant mothers do not retain a marked excess of water in the tissues. Not one of these factors, nor all of them operating together normally suffice to cause excessive water retention.

The hydræmic state of the blood.—The hydræmia facilitates the transudation of fluid from the blood to the tissues, and lowers the effective osmotic pressure of the plasma colloids. For reasons which I have suggested these two factors could not account for a progressive loss of fluid to the tissues. They might be responsible, at least in part, for the normal excess of fluid in the tissues, and might conduce to the malnutrition of the capillary endothelium. The hydræmia is normal to pregnancy and there is no convincing evidence to show that the blood becomes more diluted in those cases which evince excessive water retention. On the other hand we do know that the blood becomes more concentrated in pre-eclampsia, and in eclampsia itself the red cell count, the hæmoglobin, and the specific gravity of the blood are well above the normal levels. Finally the post-partum water diuresis occurs before any significant change occurs in the direction of blood concentration.

Sodium retention.—Sodium is indubitably retained in considerable amounts, not only during pregnancy, but apparently also during lactation. If this sodium were retained in the tissue spaces in an osmotically attractive form the woman should drown in her own tissue fluids, and unless and until it can be shown that the woman who suffers from œdema also retains more sodium in an osmotically attractive form it is illogical to attribute excessive water retention to sodium. Once again let it be noted that the post-partum water diuresis occurs while the stored sodium is still in the body.

The sex steroids.—No one can be sure of what the sex steroids cannot do. It is generally believed that the amounts of these steroids circulating in the blood tend to fall towards the latter end of pregnancy, just at the time when water retention is likely to occur. No one, so far as I am aware, has shown that they are present in increased amounts in the blood of patients manifesting œdema. The post-partum diuresis certainly accords with the view that the water is in some way held in the tissues by their operation.

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and the consequent escape of fluid into the tissue spaces. This view obtains some support from the fact that the intravenous injection of minute amounts of post-pituitary extract suffices to inhibit water diuresis in these patients.

(b) The expectant mother tends to pass more urine by night than by day.

(c) Rest in bed cures most cases of pregnancy œdema, unless the condition is associated with gross malnutrition. It is not the rest, I suggest, but the horizontal position which effects the cure, and exercise in bed could but aid the process.

(d) Ankylostomiasis is not usually associated with œdema, but up to 90% of all gravid women who are heavily infected with this parasite show not only œdema, but also anasarca.

(e) Water retention is more common in association with primiparity and multiple pregnancy.

(f) Water diuresis occurs shortly after delivery when the blood is still hydræmic and the sodium is still retained. Unless it can be shown that the sex steroids directly cause the retention of water in the tissue spaces, this one fact almost proves that mechanical factors are those which actually determine the water retention of pregnancy.

Once the excess water stored in the tissues by day ceases to escape by night, abnormal retention can proceed at an alarming pace. The slightest alteration in the permeability of the capillary endothelium, whether caused by malnutrition due to venous stagnation, or to general malnutrition, might result in a very rapidly extending œdema, and the œdema fluid might contain considerable amounts of protein. It is only necessary to call to mind the heavy albuminuria which may be occasioned in susceptible subjects by the sudden adoption of the upright position, to realize the catastrophic effects which might result from small changes in the permeability of the capillary endothelium. The constant wonder to me is that pregnancy is ever normal.

I would suggest that a well-balanced, easily digested, and attractive diet, containing plenty of first-class proteins, and adequate amounts of the vitamins and necessary minerals; plenty of exercise, well-emptied bowels, and a healthy mind are the best means of preventing excessive water retention. Theoretically it is important to limit the intake of table salt and sodium bicarbonate, and although many authorities consider this important I have never found it necessary. The water balance may be restored in three different ways; by limiting the intake of water, by diuretics, and by increasing the period of "rest" on the back.

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Mr. W. C. W. Nixon: *Water metabolism in pregnancy*.—œdema in pregnancy is one of the main clinical manifestations of abnormal water metabolism. The type of œdema seen in non-toxæmic women has not received enough attention. In Hong Kong, in the year 1936 (Nixon 1938) the incidence of œdema was 16.3% of admissions to the University Obstetric Clinic. Of these 210 cases (9.3%) had œdema, without toxæmia, lasting more than seven days at some time or other during pregnancy. Only those women who had a systolic blood-pressure below 130 mm.Hg. and were free from albuminuria were included in the investigation. Certain conclusions were reached. There was no significant difference between: (1) The duration of œdema and parity; (2) the systolic blood-pressures of primigravidae and multigravidae; (3) the average blood-pressure of the œdematous group and the non-œdematous control group; and (4) the onset of œdema was not associated with a rise in blood-pressure.

On my return to this country in company with Drs. Wright and Fieller (1942) a small group of cases (14) of non-toxæmic pregnancy œdema were investigated for vitamin B₁ deficiency. We did not find any significant difference in the vitamin B₁ excretion between this group and the controls. Apart from toxæmia the most

impressive clinical example of abnormal water retention is to be seen in pregnancy complicated by beri-beri. Professor Gordon King's (1941) report on the work in the Hong Kong University Obstetric Clinic is of particular interest. The following table is taken from this report and shows the deaths due to beri-beri.

DEATHS FROM BERI-BERI IN PREGNANCY

(Hong Kong University, 1940)						
Pyruvic acid	Age	Gravida	Maturity	Œdema	Duration	Onset
—	20	1	?	Legs	5½ months	—
—	24	2	38	Legs	1½ months	—
—	25	1	40	Legs	1 month	—
—	28	1	36	Extremities	—	—
—	—	—	—	Abdominal wall	3 months	—
1.45	24	2	40	Legs	1½ months	—
—	22	1	38	Abdom., legs	1½ months	—
—	27	2	38	Legs	3 weeks	—
2.70	40	9	39	Legs	2 months	—
2.40	28	4	43	Legs	1½ months	—
0.96	36	5	35	Legs	2 months	—
0.93	25	1	39	Legs	—	—
0.85	28	4	40	Legs	4 months	—
0.80	21	1	?	General	3 months	—
0.60	22	1	33	Legs	2 months	25th week
1.10	36	5	40	Legs	1 month	—
0.49	23	5	32	Legs	1½ months	26th week
—	34	9	29	Legs	1 month	25th week

I have analysed this table in an attempt to demonstrate the super-added strain of pregnancy in a malnutrition state. It is in consideration of these deaths that an important fact emerges, namely, the duration of œdema. The maximum duration was five and a half months and the minimum three weeks; in most women it was for one or two months. Three of the deaths were as early as the 29th, 32nd and 33rd week respectively and what is interesting in these is that the œdema was first noticed at an early stage, namely, the 25th, 26th and 25th week respectively. These cases showed the strain of pregnancy early and with this death took place at an earlier date than in the rest of the group.

Professor King has extended this study of œdema and has classified such cases into three groups (a) those associated with pregnancy toxæmia, (b) those associated with avitaminosis B₁, (c) those not accompanied by signs of either pregnancy toxæmia or avitaminosis B₁. The paper he and Professor Ride (1945) published in which they reviewed 371 cases of beri-beri complicating pregnancy merits careful study. They advanced arguments to support the view that a causal relation exists between a deficiency of vitamin B₁ and the occurrence of pregnancy toxæmia. I will quote their concluding paragraph: "Prophylaxis and/or active treatment by the exhibition of adequate amounts of vitamin B₁ whether in the form of a vitamin-rich diet or as thiamine medication, is suggested as perhaps the most important single measure dealing with pregnancy toxæmia in any of its forms."

An extensive literature has accumulated concerning water balance in pregnancy. Arnell and Guerriero (1942) have investigated a group of 500 pregnant women who presented varying degrees of œdema. Some could be explained as cardiac, renal, toxæmic in origin, others as inflammatory or mechanical—thrombophlebitis, angio-neurotic œdema, varicose veins. Other predisposing factors were hot weather, dependent position, excessive ingestion of salt and water. But there was one very interesting group in which hypoproteinæmia and anæmia were present. I would suggest that in those cases where there is œdema of the vulva without hypertension or albuminuria the serum protein should be estimated. I take for granted that the Hb of every expectant mother is examined as a routine. Dexter and Weiss (1941) found unequivocal signs of œdema of the face or hands or both between 32nd week and term in 64% of a hundred consecutive normal pregnant women. In 7% of the normal pregnant women with generalized œdema, symptoms such as frontal headaches, visual disturbances, nausea and vomiting—similar to the symptoms in pregnancy toxæmia or in severe premenstrual œdema—were noted. There was a close relation between the cerebral symptoms and the daily appearance of facial œdema.

I am relieved that even these authorities find that the mechanism of œdema of normal pregnancy, like that of pre-eclampsia and eclampsia, cannot be explained by any of the usual causes for œdema formation. By exclusion, they suspect a chemical or hormonal aetiology resulting in retention of water and electrolytes in the tissues. Of course, towards the end of pregnancy there is a physiological hydræmia with consequent reduction in protein, hæmoglobin and other blood constituents. But this will not explain the œdema that sometimes develops in normal pregnancy before the last

trimester. The clinical manifestations of excessive menstrual œdema, excessive œdema of normal pregnancy and excessive œdema of mild, pre-eclamptic toxæmia are frequently quite similar.

Site of œdema.—The feet and hands are common places for œdema and the explanation is probably postural. The vulva I have already mentioned and the need to estimate serum proteins when this region is involved. The face and eyes are influenced by gravity; here the œdema is worse in the morning after recumbency. With assumption of the upright position œdema of the face subsides and ankle œdema becomes more noticeable. I find that examination of the conjunctiva is often neglected; there will be found the tears that do not run. By pressing on the lower eyelid the subconjunctival œdema can be easily seen.

Treatment.—In prophylaxis the two most important items are dietetic, namely, a high protein but a salt-free diet. Every pregnant woman should have at least 100 grammes or more of protein daily and most of this should be first-class. Unfortunately there are still antenatal clinics where women are put on a protein-free diet for weeks on end because they exhibit either a slight hypertension, albuminuria or œdema. Nothing but harm can result from this. Strauss (1935) has conclusively shown the beneficial effect of protein in pregnancy toxæmia. We should insist more firmly on a salt-free diet during pregnancy. de Snoo (1937) has claimed that without sodium chloride retention there is no eclampsia. All indigestion powders and mixtures containing sodium should be vetoed. Likewise the diabolical habit that women in this country have of cooking vegetables with soda is to be condemned. By this practice not only do they destroy all the vitamin C but expose themselves to the risk of water retention.

Slight œdema will sometimes disappear when alkalis are given. Green-Armytage (1936) has treated cases of transient œdema successfully with daily doses of $\frac{1}{4}$ or $\frac{1}{2}$ oz. of bicarbonate of soda and potassium citrate. Again I would emphasize that potassium and not sodium salts should be used. Diuretics such as potassium or ammonium chloride can also be used. Mercurial diuretics in my experience are contra-indicated as I have known them to induce albuminuria.

Moderate or excessive œdema needs more energetic treatment. Bed is essential. By eliminating the effect of dependency and physical exercise improvement will follow. A fluid intake and urine output chart is of paramount importance. It is a mistake to flood a "waterlogged" patient with fluid, particularly intravenous saline, as is still being practised. For the first twenty-four hours I restrict the fluid intake to 500 c.c. of 30% glucose and increase the intake to 50 c.c. less than the previous day's output. The caloric value of the diet should be between 1,200 to 1,500 and consist mainly of sugar, skimmed milk, vegetables and fruit (if available).

Intravenous glucose (50 to 100 c.c. of 50% solution 6-hourly) is recommended until diuresis has been established. When glucose is being given vitamin B₁ is especially indicated. This vitamin is necessary for the oxidation of intermediate metabolites—pyruvic acid—in carbohydrate metabolism. In its absence there is incomplete combustion of carbohydrate. This is what happens in beri-beri.

Whenever diuresis is being induced the body suffers from vitamin depletion. Dr. Frederick Prescott of the Wellcome Foundation suggests that during the period of diuresis vitamins should be given daily in the following amounts: Vitamin B₁ 10 mg.; vitamin C 300 mg.; nicotinic acid 100 mg.; riboflavin 5 mg.

Vitamin C in large doses is known to have a diuretic effect and nicotinic acid has a strong vasodilator action. Recently malarial headache has been relieved by nicotinic acid (100 mg.). These headaches are due to slowing of rate of cerebral blood with resultant venous congestion, focal cerebral œdema and anoxia. I suggest that there may be a place for the use of this vitamin in pregnancy toxæmia. It relieves arteriolar spasm.

Finally, there is a place for plasma transfusion if hypoproteinæmia is an ætiological factor. A plasma transfusion of 500 c.c. is equivalent to 40 grammes of protein.

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[March 15, 1946]

The Problem of "Postmaturity"

By A. J. WRIGLEY

THE problem of "postmaturity" is not new. F. J. Browne (Ballantyne and Browne, 1922) says the problem is as old as the hills and has been noted in many ancient civilizations.

Unfortunately most of us assume that if any pregnancy continues over the calculated date for its termination, the fetus will become so large as to give rise to difficulty in its delivery. That this is not the case has long been recognized.

In 1902 Ballantyne noted that a baby weighing more than the usual number of pounds may be born at the normal time. Twenty years later he and Browne wrote: "There is no proof that if the weight of the postmature baby is near the average (as it sometimes is) the labour will be more dangerous than usual." And in 1938 Neon Reynolds told us that: "Postmaturity has peculiar difficulties as a subject for discussion, since we have at present no definition of what we mean. . . . Foetal development, well above the average as regards size, weight, ossification, &c., is not necessarily a result of prolonged gestation, just as immaturity is not synonymous with prematurity."

Adair (1940) writes: "There are individuals who persistently delay in the normal onset of labour, each pregnancy being of a longer duration than the average normal, the fetal size appearing to have no bearing on this phenomenon. The fetus may be over-size, of normal or below normal weight."

In the year 1945 there occurred some thousand deliveries in the St. Thomas's Obstetric Unit. The following tables well illustrate my point.

We first collected all those cases of women who were delivered of a baby weighing 9 lb. or over (Table I).

TABLE I.

No. of cases	Weight of babies		Estimated maturity in days \pm			
	lb. oz.	lb. oz.				
9	9 0	9 3	+18, +16 + 8, + 4 + 4	-2, -4, 0	-3 -20	
5	9 4	9 7	+40, +13 + 5	-8,	-5	
6	9 8	9 11	+ 6, + 4 + 4, + 3 + 1	0		
6	9 12	9 15	+13, +12 + 7, + 6	-2,	-3	
3	10 8		+16, +12	-5		
1	10 13			0		
1	12 0		+24			

We next estimated the weight of the babies delivered more than seven days after the calculated date (Table II).

TABLE II—BABIES' WEIGHT.

No. of cases	No. of weeks "postmature"	No. at birth weighing:					
		5 lb.	6 lb.	7 lb.	8 lb.	9 lb.	Over 9 lb.
16	1	0	5(1)*	3	5	3	0
43	2	2	6	10	11(1)*	5	0
18	3	1	7	6	2	1	0
8	4	1	2	3	2	0	0
4	5	0	2	0	2	0	0
Total 89							

*Stillbirth

Note how frequently a large healthy baby is born before the calculated date and secondly, how often a small baby, or one of normal weight, is born after the expected date. I must add that all these women had been observed throughout their pregnancies, and the expected date was calculated not only from the date of the last menstrual period but was correlated with the time of the onset of quickening and with regular observations in the rate of enlargement of the uterus.

Similar advice can be found in a few textbooks. In the Queen Charlotte's Textbook of Obstetrics (1939) we read: "There is no exact time for gestation. An apparently full-time child born 207 days after marriage has been held by law to be the legitimate off-spring of its parents. A child born 331 days after its mother's husband had left the country was held to be legitimate." Berkeley, Bonney and MacLeod (1938) in "The Abnormal in Obstetrics" mention a child "undoubtedly 6 weeks postmature" which weighed less than 5 lb. at birth. R. W. Johnstone (1937) in his Textbook of Midwifery writes: "That pregnancy followed by the birth of a fully developed child may be prolonged or

abbreviated is an observed fact. The usual explanation is a miscalculation as to dates." Fairbairn (1928) stated that: "In many cases of prolonged gestation the foetus is only of average development, and many cases of postmaturity are not accompanied by increase in the duration of pregnancy." From America, Henricus Stander in Williams' *Obstetrics* (1936) advises us that: "In the majority of cases of supposed prolongation, the delay is only apparent and the child does not greatly exceed the average."

The above extracts were collected from a search in the current textbooks of obstetrics. In most of the remainder, and they constitute the great majority, either the subject is ignored or the reader led to believe in the words of the Ten Teachers (1938) that the best evidence of a real prolongation of the period of utero-gestation is an abnormal length and weight of the infant. Likewise Munro Kerr (1937) states that: "In protracted gestation, without doubt, the child frequently suffers, and even dies", and lastly Berkeley (1938) wrote: "The average duration of pregnancy being estimated as 280 days from the first day of the last period, if the pregnancy is prolonged 10 days over such a calculation the child may be deemed to be postmature. In such cases the child is always above the average length and, most frequently, above the average weight. The head is larger and harder than normal, giving rise to difficult labour, during which the child may perish." This last is indeed a grave warning.

I maintain that we have consistently ignored the advice given us in the first series of quotations and have based our definition of postmaturity on the lines of the last three extracts, viz. that a baby born after the expected time will be large, that a baby born before the expected time will be small and that a baby born at the expected time will be "normal" in weight.

Certainly we have educated the laity on these lines. The fact that the baby has not come on the expected date is almost always likely to create a sense of anxiety which increases as one day (or week) follows another. Anyone who questions a student at the final examinations on this subject cannot fail to acknowledge that either the student has never heard the problem discussed at all, or, should he or she have been educated at one of two London Medical Schools, the answer given is to the effect that when fourteen days have elapsed labour should be induced. This reply is as fatuous as it is dangerous.

I will now turn to the question of the Diagnosis of Postmaturity.

Brown, in "Antenatal and Postnatal Care" (1944), and in the paper of 1922 already referred to, discussed the following points:—

(1) A careful scrutiny of menstruation with special reference to women who constantly miss one or more periods.

(2) Valuable evidence from the date of quickening.

(3) The foetal head; its size, its hardness, the mobility of the skull bones, the width of the sutures and fontanelles, may be estimated with a fair approach to accuracy by the examining finger in the vaginal fornices or by palpating the head through the open cervix.

(4) Foetal mensuration: "No method is sufficiently accurate to be of use in clinical practice."

(5) Cephalometry by X-rays: "It is possible by measuring the size of the foetal skull by means of X-rays to arrive at a more or less accurate estimate of the size and weight of the foetus."

This table is accepted for the most part by other authors such as Masters and Clayton (1940), Reynolds, the Ten Teachers and Cameron (1939).

As variants Jellett (1930), Comyns Berkeley and Titus in America (1940), suggest that the diagnosis is made on the fit of the foetal head into the pelvic brim. Jellett and Madill (1929) advise "the length of the foetal ovoid can be directly measured by placing one blade of the calipers on the pelvic pole of the foetus *per vaginam*, and the other blade on the abdominal wall in close contact with the fundal pole".

Herman (1939) and Henricus Stander deny that the foetal head is likely to be of much help in the making of the diagnosis, and the former points out a fact of considerable clinical importance when he adds that in the case of large babies, whose intra-uterine development is excessive, the shoulders are larger in comparison with the head than is normal and with such a child the excessive size of the shoulders may greatly obstruct delivery. Fairbairn advised that it virtually was not possible to make the diagnosis of postmaturity during pregnancy as there was no accurate method of determining the size of the foetus. Berkeley and Bonney seem to agree with this and suggest the diagnosis usually is suspected during an obstructed labour and confirmed when the baby has arrived. I was unable to discover any mention of the diagnosis in the books written by Bourne (1941), Gibberd (1938), Johnstone, Munro Kerr or in the Queen Charlotte's Textbook.

From the above evidence the question will now be criticized collectively, and, according to the symptoms and signs, individually. Collectively you must agree the outlook is discouraging. The advice is contradictory or absent. Individually each symptom or sign fails to be absolute, and by itself never more than suggestive. The reason for these facts surely rests on exactly the same faults as we saw applied to the difficulties that arose on the question of the definition of the condition. Nearly every author has written on the assumption that postmaturity must be the synonym for what Herman termed excessive intra-uterine development of the foetus, and yet most of them knew that this was not the case.

Lastly in this respect I would refer to the failure of radiography to help in the diagnosis.

Browne writes: X-rays are of little help, though the existence of a very large ossific centre in the cuboid would be confirmatory evidence of postmaturity"; but the following sentence reads: "The ossific centre may, however, be of this size without the foetus being postmature(!)." Gibberd agrees and believes that "there is such wide variation in the times of appearance of the ossific centres that they are of little use in this connexion". Reece (1935) suggested that the maturity of the foetus could be calculated almost to the day by means of foetal cephalometry. He was answered by Reynolds in the words: "It is difficult to believe that any diameter is such a fixed factor that it is possible to say, because the diameter is 3.75 inches that therefore the foetus is of 40 weeks' maturity". Are we all then made alike?

Munro Kerr stating that he does not feel sufficiently experienced to pronounce judgment on foetal cephalometry most rightly proceeds: "I would, however, say this, that it will never be possible to estimate mouldability of the head, minor adjustments of the head to the pelvis, and the power of the expulsive forces, which are of primary importance in determining whether the head will or will not pass through a pelvis."

I would value Fairbairn's advice as the most valuable but he omitted to give us the reason for his statement, which should have been followed by a sentence to the effect that a postmature baby need not be unduly large and a premature baby is not, of necessity, unduly small.

Treatment or management.—This makes even more depressing reading and again I must quote freely.

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Several authorities are more definite on their advice as to when induction should be performed. Browne says: "While, however, it would be strictly speaking, correct to term a woman postmature if she has gone more than eight days past her expected date, it would be absurd to class her as abnormal, and therefore needing treatment. She could only be considered abnormal if she were exceptional and it is certainly not abnormal for a woman to go eight days past her estimated date of delivery. A good clinical rule is that she should not be allowed to go more than a fortnight past her estimated date, always provided that these dates have been correctly ascertained." My criticism of the above is that the reader would certainly interpret the advice as never induce at the eighth day and always by the fifteenth day after the expected date (correctly ascertained). This interpretation is fraught with danger, for the baby may easily be more truly postmature on the eighth day than it is on the fifteenth, and I venture to agree with Browne himself that "dates" are more notoriously misleading. Queen Charlotte's Textbook repeats Browne's advice with: "Labour should be generally induced whenever a patient is more than a fortnight overdue." Nothing else is said and can the student be blamed if he regards this as dogma?

Berthel Solomons advises induction at the 40th week provided that "it is certain that the date is correct (it never is certain) and if the head just fits the brim". The foetal head may be deep in the pelvis and yet the foetus be grossly postmature and of a dangerously large size.

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Masters and Clayton are definitely against a routine induction of labour. "It would seem unjustifiable to induce labour in patients who are thought to be postmature, but in which there is no evidence of disproportion for the following reasons: (1) The un-

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Masters and Clayton are definitely against a routine induction of labour. "It would seem unjustifiable to induce labour in patients who are thought to be postmature, but in which there is no evidence of disproportion for the following reasons: (1) The un-

abbreviated is an observed fact. The usual explanation is a miscalculation as to dates." Fairbairn (1928) stated that: "In many cases of prolonged gestation the foetus is only of average development, and many cases of postmaturity are not accompanied by increase in the duration of pregnancy." From America, Henricus Stander in Williams' Obstetrics (1936) advises us that: "In the majority of cases of supposed prolongation, the delay is only apparent and the child does not greatly exceed the average."

The above extracts were collected from a search in the current textbooks of obstetrics. In most of the remainder, and they constitute the great majority, either the subject is ignored or the reader led to believe in the words of the Ten Teachers (1938) that the best evidence of a real prolongation of the period of utero-gestation is an abnormal length and weight of the infant. Likewise Munro Kerr (1937) states that: "In protracted gestation, without doubt, the child frequently suffers, and even dies", and lastly Berkeley (1938) wrote: "The average duration of pregnancy being estimated as 280 days from the first day of the last period, if the pregnancy is prolonged 10 days over such a calculation the child may be deemed to be postmature. In such cases the child is always above the average length and, most frequently, above the average weight. The head is larger and harder than normal, giving rise to difficult labour, during which the child may perish." This last is indeed a grave warning.

I maintain that we have consistently ignored the advice given us in the first series of quotations and have based our definition of postmaturity on the lines of the last three extracts, viz. that a baby born after the expected time will be large, that a baby born before the expected time will be small and that a baby born at the expected time will be "normal" in weight.

Certainly we have educated the laity on these lines. The fact that the baby has not come on the expected date is almost always likely to create a sense of anxiety which increases as one day (or week) follows another. Anyone who questions a student at the final examinations on this subject cannot fail to acknowledge that either the student has never heard the problem discussed at all, or, should he or she have been educated at one of two London Medical Schools, the answer given is to the effect that when fourteen days have elapsed labour should be induced. This reply is as fatuous as it is dangerous.

I will now turn to the question of the Diagnosis of Postmaturity.

Browne, in "Antenatal and Postnatal Care" (1944), and in the paper of 1922 already referred to, discussed the following points:—

(1) A careful scrutiny of menstruation with special reference to women who constantly miss one or more periods.

(2) Valuable evidence from the date of quickening.

(3) The foetal head; its size, its hardness, the mobility of the skull bones, the width of the sutures and fontanelles, may be estimated with a fair approach to accuracy by the examining finger in the vaginal fornices or by palpating the head through the open cervix.

(4) Foetal mensuration: "No method is sufficiently accurate to be of use in clinical practice."

(5) Cephalometry by X-rays: "It is possible by measuring the size of the foetal skull by means of X-rays to arrive at a more or less accurate estimate of the size and weight of the foetus."

This table is accepted for the most part by other authors such as Masters and Clayton (1940), Reynolds, the Ten Teachers and Cameron (1939).

As variants Jellett (1930), Comyns Berkeley and Titus in America (1940), suggest that the diagnosis is made on the fit of the foetal head into the pelvic brim. Jellett and Madill (1929) advise "the length of the foetal ovoid can be directly measured by placing one blade of the calipers on the pelvic pole of the foetus *per vaginam*, and the other blade on the abdominal wall in close contact with the fundal pole".

Herman (1939) and Henricus Stander deny that the foetal head is likely to be of much help in the making of the diagnosis, and the former points out a fact of considerable clinical importance when he adds that in the case of large babies, whose intra-uterine development is excessive, the shoulders are larger in comparison with the head than is normal and with such a child the excessive size of the shoulders may greatly obstruct delivery. Fairbairn advised that it virtually was not possible to make the diagnosis of postmaturity during pregnancy as there was no accurate method of determining the size of the foetus. Berkeley and Bonney seem to agree with this and suggest the diagnosis usually is suspected during an obstructed labour and confirmed when the baby has arrived. I was unable to discover any mention of the diagnosis in the books written by Bourne (1941), Gibberd (1938), Johnstone, Munro Kerr or in the Queen Charlotte's Textbook.

From the above evidence the question will now be criticized collectively, and, according to the symptoms and signs, individually. Collectively you must agree the outlook is discouraging. The advice is contradictory or absent. Individually each symptom or sign fails to be absolute, and by itself never more than suggestive. The reason for these facts surely rests on exactly the same faults as we saw applied to the difficulties that arose on the question of the definition of the condition. Nearly every author has written on the assumption that postmaturity must be the synonym for what Herman termed excessive intra-uterine development of the foetus, and yet most of them knew that this was not the case.

Lastly in this respect I would refer to the failure of radiography to help in the diagnosis.

observer has been watching the particular patient at regular intervals throughout her pregnancy and at frequent intervals throughout the later weeks. For instance, whereas the amount of liquor amnii varies considerably in different women, in all women there should be a relative, and as full time is reached, a noticeable apparent decrease in amount. Emphasis is laid on this last sentence. As an example could be cited the multipara who as a result of many pregnancies has a poor abdominal musculature, a lax toneless uterine wall and very often a tendency to slight hydramnios. The casual observer, seeing this patient at the estimated 42nd week of pregnancy, could not possibly be expected to say that the uterus contains "a more easily palpated foetus" or "an apparently decreased amount of liquor". If, however, this patient has been observed regularly by the same person, both these findings, which it is held, are of considerable importance, may be recorded with confidence. No other physical sign, or symptom, is put forward for consideration. It is contended that all the remainder are not only of little use but may actually be misleading.

At this point a plea is made for a complete revision of many of our ideas on pregnancy and its termination. At the present time each patient is given an "expected date". This date is necessary, because probably it will be fairly accurate, and because many and various arrangements have to be made for the forthcoming confinement. But at the same time let us be more careful always to explain to our patients that, at the best, the date may be only approximate and that the baby may arrive before or after, perhaps considerably after the expected time. Also let us say at once that it will probably never be possible at any time during the pregnancy to make a more accurate forecast.

On or about the "calculated date" it is expected that the woman will start her labour and produce a healthy baby weighing about 7 lb. These two events do in fact take place in the majority of patients. But in quite a considerable minority variations occur. These variations are three in number and as each one is of the greatest importance they deserve emphasis.

First, the expected date may come and go and the labour start some days or weeks later with the delivery of a large postmature baby. Secondly, the expected date may come and go and the labour start some days or weeks later with the delivery of a normal-sized baby (that is to say, about 7 lb. in weight and 20 in. in length) or even of a baby that is even less in both weight and length. Thirdly and lastly, at or about the time of the calculated expected date, or even earlier, the labour starts and the woman is delivered of a large, oversized baby that shows every characteristic attributed to postmaturity.

Now, as I have already stated, it is accepted by the laity, and by the great majority of the medical profession that a baby born before the expected date will be smaller than the normal, that a baby born at the expected date will be of normal dimensions and that a baby born after the expected date will be larger than the normal. Such is usually, but by no means always, the case. The Irish members of the audience will appreciate what is meant, when it is stated that a postmature baby may well be born prematurely and a premature baby may arrive after the calculated 40 weeks have come and gone.

A lack of appreciation of these facts results in a great deal of anxiety on the part of the lay public and of their medical attendants and as a result leads also to a deal of bad midwifery. Thus it is just as important to try to realize that when the expected date of confinement has been passed, the foetus may not necessarily be mature as it is to realize that it may be, and perhaps dangerously so, postmature.

Attention has already been drawn to the difficulties in diagnosis and to the absence of, or at the best, the most indefinite assistance given on this subject in the current textbooks of obstetrics. Because of this the medical attendant adopts one of two courses. Either every woman who passes the calculated date of confinement receives a medical induction, or, in the realization that many "postmature" babies are not unduly large, the rule of "leave it to Nature" is adopted with the result that occasionally the wretched patient delivers herself of a large truly postmature baby, perhaps with great difficulty and considerable risk to herself and to the baby. Both courses are equally reprehensible. Furthermore there is no justification whatever for advising that a week or a fortnight should be allowed to elapse after the expected date has passed and at that time if labour has not started the labour should be induced. If this advice is followed, in the first place a number of women will go into labour later than they should be allowed to do and true postmaturity be ignored, or alternatively the baby may well, even at the calculated 42nd week, not be mature.

Another great objection to this plan is that all too often it leads to repeated medical inductions. Apart from the inevitable physical upheaval of such proceedings which

certainly of any diagnosis of postmaturity; (2) the lack of any definite evidence that placental degeneration causes foetal death; (3) the risk of inertia." While I would be prepared to agree with this advice, much more constructive help can be given.

In three American textbooks, however, we find much more encouragement. Titus, after a short summary on the assessment of a large foetus in which he draws attention to the size of the abdomen, the size and hardness of the foetal head and the danger of the large shoulder girdle, advises that: "When it can be demonstrated that the fetus is large and the available evidence indicates that labour is overdue, its induction is indicated." Stander writes: "If the patient has gone beyond term and the examination shows that the size of the child is above average, there should be no hesitancy in the induction of labour as a prophylactic measure. On the other hand, if the child is small, induction should not be thought of. Excessive size of the child is rarely suspected by the ordinary practitioner before the onset of labour and the diagnosis is only made after Nature has shown that she is unable to effect delivery. If the patient is carefully palpated at intervals during the last months of pregnancy and weekly if the child is not born within one week of the calculated date of delivery, excessive size of the child will rarely escape recognition." Both these writers have advised that the size of the foetus is not necessarily proportionate to the duration of the intra-uterine gestation.

Adair's advice is even more practical. He writes: "In our clinic no definite regime of treatment is followed. Each case is evaluated individually and therapy instituted depending on the conditions found present. Ordinarily it is expectant, the patient being examined each week for excessive size of the fetus and untoward signs. If none be present, she is usually allowed to continue with the pregnancy until natural onset of labour, this being time and again found to be the course least fraught with danger of complications." Note the stress by both the last writers laid on the necessity of the repeated frequent examinations and by the last writer that each case should be judged on its merits. Reynolds sums up these last views with his words: "Is it necessary to have a standard? Is treatment required simply and solely because a pregnancy appears to have continued beyond what we regard as its average duration?"

From what has been quoted it may be fairly stated that little help has been offered to the student or practitioner, at any rate, by British writers. An accurate and more careful assessment of the dates of the last normal menstruation is often advised. The estimation of the height of the fundus will never assist—especially in the last weeks of pregnancy. Girth measurement varies enormously in different women and in any case this measurement does not necessarily increase greatly when the foetus is postmature—this because there is no corresponding increase in the amount of liquor amnii. The engagement or non-engagement of the foetal head at or after term need not help. The foetal head of the truly postmature foetus will stay deeply engaged and low in the pelvic cavity and what is perhaps more misleading, a foetal head that is doubtfully engaged at or about term may easily sink lower as the foetus increases in size to become postmature. The initial hopes that some definite aid might be expected from radiography were soon dashed. Critical observations revealed great variation in the appearance of the various centres of ossification.

The following additional physical signs are put forward to be used in conjunction with pointers that may or may not be present in any of those just mentioned:

(1) When the foetus is truly postmature it is large. Its weight is well above 7 lb. This unusual size can be appreciated on repeated clinical examinations.

(2) Concurrent with the increase in size, is increase in strength. Foetal skeletal muscles develop rapidly in the latter weeks of pregnancy and it is my impression that this development increases even more rapidly in the postmature foetus. Now as these muscles develop, so does the increase in muscle tone become more noticeable. This increase in muscle tone results in the whole foetus becoming more rigid. It is suggested that this rigidity can be recognized on clinical examination. So far, therefore, we have a large foetus and a rigid foetus.

(3) The quantity of liquor amnii in the amniotic sac normally does not appear to increase in the last weeks of pregnancy. One result of this is that as the pregnancy advances it becomes more and more easy to palpate the foetus. In true postmaturity it is often the case that the uterus may be said to be "full of foetus". There is relatively little liquor amnii and everywhere in the uterus there is to be felt some part of the foetus. Thus there may be, and in fact, often there is present a large rigid foetus easily felt in a uterus that contains relatively little liquor, perhaps so little that the uterine wall may be justifiably imagined to outline the foetal position and some of its limbs.

While these signs may be quite obvious, in certain instances, this is not the rule. Their onset and their observation will only be made with reasonable certainty if the

[May 17, 1946]

Full-term Abdominal Pregnancy.—MARY KATHLEEN LAWLOR, F.R.C.S.Ed.

Full-term abdominal pregnancy, occurring in a healthy young primipara, with no history of tubal rupture or vaginal losses during pregnancy, is suggestive of a primary abdominal cyesis.

The mother, aged 26, attended the ante-natal department for the first time in November 1945 at 38 weeks' maturity, with a letter from her doctor stating that the foetus was lying transversely and that he had made two unsuccessful attempts to perform a version. The pregnancy had been complicated by attacks of diarrhoea and vomiting which had always been diagnosed as enteritis.

On examination, it was not difficult to decide that the foetus lying transversely in the upper abdomen was extra-uterine. There was a rounded sub-umbilical swelling which was diagnosed as the placenta and, on vaginal examination, a normal non-pregnant uterus was found lying posteriorly to the placental mass.

Abdominal section confirmed the diagnosis. A perfectly healthy female infant weighing 7 lb. 6 oz. was extracted through a rent in the mesentery. It was lying free in the peritoneal cavity with no liquor amnii. The placenta presented as a highly vascular globular swelling attached to the anterior abdominal wall and the pelvic organs, the view of which it entirely obscured. The umbilical cord was traced to the left-hand corner of the placenta where the foetal membranes were also attached.

Every effort was made to avoid separating the placenta, the vessels of which were of an alarming size, and the abdomen was closed without drainage.

The puerperium was uneventful. The wound healed by first intention. Efforts to establish lactation were unsuccessful and there was no vaginal loss of any kind until the 5th week of the puerperium when an apparently normal period occurred, but was unusual in that it persisted for five weeks. Since then normal monthly periods have taken place, but the 4th and 5th have been a little heavier than usual.

Attacks of diarrhoea and vomiting continued to occur from time to time over 4 months and the patient's general condition was not satisfactory, although the only complaint was tiredness and the only sign the persistent swelling of the placenta left in situ.

This swelling did not show any attempt to decrease in size until the 5th month. There were no signs of calcification or inflammation. The patient began to feel stronger and healthier with the decrease in size of the placenta, which is to-day, May 17, 1946, a tensely, non-tender, cystic swelling about the size of a 14 weeks' cyesis which will presumably disappear by a process of necrosis, liquefaction and absorption.

The baby which is now 6 months old is thriving satisfactorily and is an exceptionally bright and attractive child.

Endometriosis of the Colon.—H. R. ARTHUR, F.R.C.S.Ed.

An unmarried woman, aged 31, complained of pain "all over" the lower abdomen, which she had had with increasing severity for the previous two years. Nothing relevant in her past history. Menstrual history normal, being a 5 day loss in a 28 day cycle, but she stated that she had always had a heavy flow and dysmenorrhoea, and the pain was worse at the time of the menstrual period. The menstrual flow, however, had been no heavier than usual in spite of the extra pain. At the menstrual period, too, her motions were loose and accompanied sometimes by slight bleeding *per rectum*. She had no other symptoms and was able to work as a V.A.D. nurse.

On examination.—Healthy-looking woman with no clinical anaemia; abdomen tender in both lower quadrants, more marked in the left. No mass was palpable. Pelvic examination revealed a normal uterus but with slightly restricted mobility, due to pain. A tender, hard, fixed, irregular mass was palpable in the left side of the pouch of Douglas, apparently adherent to the rectum. The right fornix was clear, the lower genital tract showed no abnormality. All other systems were normal.

Diagnosis.—Pelvic endometriosis with a second differential diagnosis of carcinoma of the ovary.

involve the administration of a stiff dose of castor oil, the induction is accompanied by a variable degree of anxiety which is not alleviated by frequent injections of pitocin and this anxiety is definitely and inevitably increased by each repeated failure to cause the onset of labour. In addition should the induction succeed a considerable proportion of the babies born will be premature although the calculated 40th week was passed. I insist that we should institute a rule in our practice and in our teaching, that if there is a justification for medical induction of labour there is a justification for surgical induction. The full and tedious routine of a medical induction is fully justified when there is a considered necessity for it and should only be embarked upon when the medical attendant has accepted this rule and automatically will perform a surgical induction within a few days of the failure of the medical induction. I have followed this procedure in my own practice, in and out of hospital, for some years and have found no cause to regret doing so.

I instance two very recent cases that illustrate the point I wish to make. The first is that of a primigravida aged 28, who expected her first baby on January 18. From the findings on examinations made during the preceding four to five weeks it became certain that this woman had matured what might be termed "a good strong baby". Therefore on January 18 she was given a routine medical induction. This failed and the membranes were ruptured. Although the foetus appeared large, the foetal head was deeply engaged in the bony pelvis. Labour started and after twenty-four hours she was delivered of a 9 lb. 2 oz. baby by a low forceps operation. The delivery of the shoulders was not easy. This woman might well have not gone into labour if left alone for a fortnight and the delivery then would have been longer and much more difficult. The second case was that of a woman, aged 30, who was expecting her third baby on January 1. At that time and in the preceding weeks the foetus had never appeared large. Her two previous confinements had been normal and the babies had "arrived late" and neither had weighed as much as 7 lb at birth. She was seen each week and labour started naturally on January 24. After four hours' labour she was delivered of a baby weighing 6½ lb. Both these women had been observed regularly from the beginning of pregnancy. In both of them the size of the uterus had been observed in the early months and in both cases this and the date of onset of foetal movements corresponded with the supposed date of onset of the pregnancy.

In conclusion I put the following points forward for consideration. Whereas we shall continue to give to our patients the same estimated date for the confinement, and while we continue as before to take note of the rate of increase in the size of the uterus throughout pregnancy and the time of appreciation of the first foetal movements and any other relevant symptom or sign, we do, from now onwards, cease to teach, that every woman will inevitably mature her baby of 7 lb. weight in the calculated 40 weeks. We should instruct our students that often a normal healthy woman will mature a large, or normal, or small baby in a pregnancy that may last for 40 weeks, or more, or less. Let us abolish any instructions to terminate pregnancy as a routine at the calculated 40th week, 41st week, 42nd week or what you will. Let us teach that by repeated observations at regular intervals during the later weeks of pregnancy there appears a combination of physical signs (which have been described) from which we shall receive guidance to our course of action; and that it may well be as necessary to terminate the pregnancy at the 38th week for a baby that is obviously large, as it might be at the 43rd week, or conversely that in the absence of these definite physical signs let us insist that all interference is bad midwifery. Lastly, let us forbid the administration of a full medical induction unless the indications for induction are such that its failure automatically necessitates a surgical induction.

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These tumours were first described in 1927 by Moretti and Arrigoni, and are found most frequently in women past the menopause when they give rise to vaginal bleeding. They have also been recorded in younger women complaining of irregular vaginal bleeding. They are unilateral, solid in consistency and formed of connective tissue cells rich in fat. They secrete oestrogenic hormone.

Schiller believes that these tumours arise from ovarian mesenchyme and regards them as a subgroup of fibromata. Novak, on the other hand, states that they are granulosa-celled tumours which have become luteinized. In support of this latter view, Traut and



FIG. 1.—Endometrium showing cystic hyperplasia. $\times 32$.

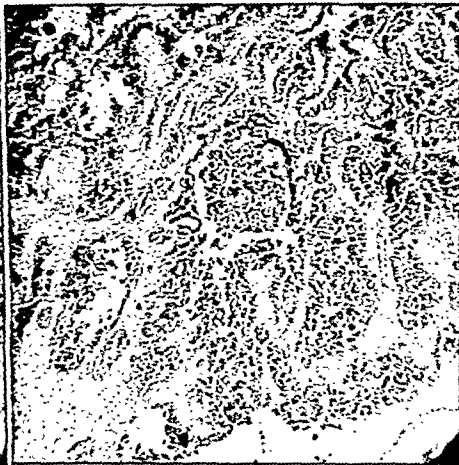


FIG. 2.—Papilliferous adenocarcinoma. $\times 32$.

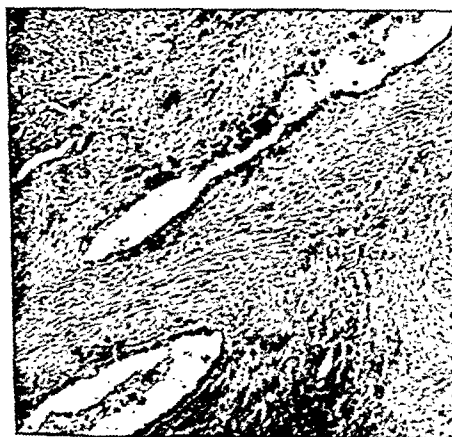


FIG. 3.—Xanthofibroma thecocellulare. $\times 184$.



FIG. 4.—Xanthofibroma thecocellulare. $\times 31$.

Note: Fig. 3.—Malignant epithelium lining the cystic spaces.

Fig. 4.—Section stained for fat which is seen in cystic spaces.

Butterworth were able to produce thecomata and granulosa-cell tumours in immature mice by irradiation of the ovaries. This subject has been reviewed by Miss Barnes.

It is a rare tumour with low-grade malignant characteristics, and this case described is of especial interest as it shows the presence of a carcinoma as well, possibly a secondary growth, the primary site of which was in the opposite ovary.

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Operation.—At operation several small scattered endometrial nodules were found on the floor of the pouch of Douglas, and the mass was seen to consist of contracted mesocolon, containing endometrial deposits together with a stricture of the bowel at the pelvi-rectal junction. The appearance of the bowel lesion itself suggested a ring carcinoma, but the presence of endometrial deposits in the mesocolon and pelvic peritoneum, together with the complete absence of secondary deposits in the liver or the abdominal cavity, failed to support this diagnosis. The affected area of colon was mobilized and a Paul-Mikulicz resection was carried out in two stages.

Recovery was uneventful; six months later patient was in very good health and back at her job.

Histological examination.—Typical endometrial tissue was found in the muscular wall of the colon.

Comment.—Endometriosis may occur without involvement of the genitalia, so that treatment of this condition may be by the gynaecological surgeon or the general surgeon.

Endometriosis of the colon may be either part of a co-existing pelvic endometriosis or, more rarely, it may be the primary site of the disease. In the first type it is usually a part of the mass of adhesions which is so conspicuous a feature of this lesion, but the wall of the colon may be invaded by ectopic endometrial tissue. The second type of case is less common and the lesion may be a constrictive one, such as the one described, or may be a localized endometrioma, two cases of this latter type being recently described by Mr. Douglas McLeod in his Hunterian Lectures before the Royal College of Surgeons. In either type the important differential diagnosis is from the carcinoma of the bowel, and this may not be made until the abdomen is opened. If a localized tumour is found it may be removed, leaving the bowel lumen intact but if, as was found in this case, a constrictive lesion is present (and the patient is a young woman) resection must be undertaken, with a prognosis, of course, very different from that of a similar case in which the lesion is malignant.

Xanthofibroma Thecocellulare, which became the Site of a Secondary Carcinoma from the Opposite Ovary.—E. W. C. BUCKELL, M.B., B.S., M.R.C.O.G.

Mrs. H., aged 66, para 4. Admitted to University College Hospital 29.12.45. Menopause twenty-four years ago. Complaining of vaginal bleeding for six days, three weeks before admission to hospital.

Examination revealed abdominal ascites and a hard, fixed mass in the pouch of Douglas.

Operation on 1.1.46 revealed bilateral ovarian tumours, measuring about 2 in. diameter with papilliferous growths on their surface. Small papilliferous growths had also invaded pelvic peritoneum. Total hysterectomy and bilateral salpingo-oophorectomy was performed and as much pelvic peritoneum as possible was removed.

Recovery was uneventful. A course of deep X-ray therapy was given about six weeks later.

Follow-up: Last seen on 1.5.46 when the ascites had recurred and in her abdomen a hard mass could be felt rising out of the pelvis.

Specimen consisted of a uterus removed by total hysterectomy together with both appendages. The uterus was of normal size and was lined by a thickened endometrium. A section showed the presence of a number of cystic glands and a dense stroma infiltrated with lymphocytes (metropathia hæmorrhagica) (fig. 1).

The left ovarian tumour measured about 2½ in. by 1½ in. and consisted, for the most part, of two cysts. One cyst measured 1½ in. in diameter and contained blood-stained fluid; there was a fine papilliferous lining. The other cyst was smaller and was not opened. The surface of the tumour was studded with rather larger papilliferous nodules. Section of the growth showed it to be a papilliferous adeno-carcinoma (fig. 2).

The right ovary was replaced by a solid yellowish-white tumour measuring about 2½ in. by 2 in. There was a small cyst at the base of the growth. The surface was also studded with small nodules.

A section showed it to have a stroma analogous to that of a fibroma. It harboured numerous cavities, most of them narrow and elongated and a few short cystic ones. They were lined by a malignant epithelium similar to that seen in the other ovarian tumour (fig. 3). Another section of the growth was stained with Sharlach red. It showed the presence of fat in degenerated cells floating in the lumen of cystic cavities, and also in the stroma cells (fig. 4). The tumour was therefore a xanthofibroma thecocellulare.

These tumours were first described in 1927 by Moretti and Arrigoni, and are found most frequently in women past the menopause when they give rise to vaginal bleeding. They have also been recorded in younger women complaining of irregular vaginal bleeding. They are unilateral, solid in consistency and formed of connective tissue cells rich in fat. They secrete oestrogenic hormone.

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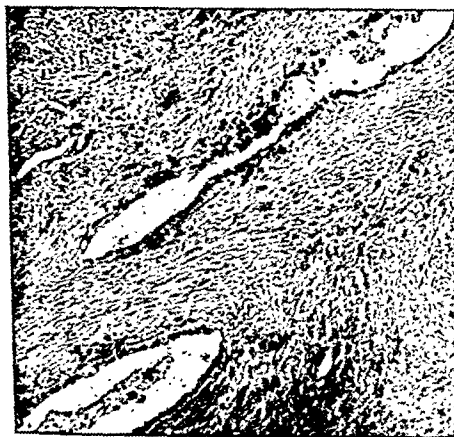


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Cervical Missed Abortion.—S. G. CLAYTON, M.S., F.R.C.S.

Patient, aged 30, married for three years. Two years previously she became pregnant, but after three months the uterus ceased to enlarge, and a missed abortion was diagnosed, and evacuated after it had been retained *in utero* for a further four months.

When first seen in January 1944 she stated that her last normal period had been in July 1943. She had slight bleeding in October, and a larger loss with quite severe pain in November. The pain and bleeding ceased, and when seen in January the uterus was of the size of a 14 weeks' pregnancy, and the external os was closed. Missed abortion was diagnosed, but as 600,000 units of œstradiol benzoate were injected without result, the patient was sent home to await spontaneous abortion.

Four months later (in May) nothing more had happened, so the patient was re-admitted. The physical signs were unchanged, and an attempt was made to dilate the cervix with metal dilators. This was astonishingly difficult, and to avoid injudicious violence the cervix was incised before the rounded solid mass of the mole was removed entire, the mass consisting chiefly of foetal bones. On passing a finger into the cavity it was alarming to find a rounded hole in what was thought to be the fundus, but further examination showed that the small body of the uterus was above, and that the mole had been removed from the grossly dilated cervical canal. The cervical incision was stitched and recovery was uneventful.

As judged by a lipiodol hystero-graph the dilated cervix returned to normal in six weeks and no cause for the recurrent abortions was found. A year later the patient became pregnant again and went uneventfully to full term, when she had a normal delivery.

Presumably the gestation was extruded from the uterine cavity at the time that she noticed pain and bleeding, but it is difficult to know why the external os failed to dilate to allow the ovum to pass, as the cervix afterwards appeared perfectly healthy. It is not surprising that œstrogens had no effect if the ovum was in the cervix. It is also curious that the menstrual cycle was not re-established until the mole was evacuated.

Accurate details of her earlier pregnancy could not be obtained, and although it is possible that that also was a cervical abortion there is no proof of that. (Masieri has reported a case in which cervical abortion occurred in two successive pregnancies.)

The condition of cervical missed abortion is clearly described in Taussig's monograph on abortion. It is to be distinguished from rare and genuine cervico-isthmal pregnancy in which the ovum is actually implanted in the isthmus or upper cervix.

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Melanoma of the Vulva with Pregnancy.—S. G. CLAYTON, M.S., F.R.C.S.

Patient, aged 27, was eight weeks pregnant in her first pregnancy. She complained of a swelling on the right labium majus, which had been present without alteration for many years. On examination a pedunculated swelling was found, about 4 cm. in diameter, firm in consistency, with somewhat thickened skin over it, but without evident pigmentation. The inguinal glands were not enlarged.

A diagnosis of pedunculated fibroma was made, and in June 1941 the tumour was excised with a fair margin of normal skin. Section unexpectedly showed that the tumour was a melanoma, consisting chiefly of spindle-shaped cells, with very little pigment, and not appearing very active. Further section of the pedicle showed no tumour cells. In view of this fact, and the long history of the tumour, inguinal dissection was not performed, and radiation was not used because of her pregnancy. Her labour was uneventful.

Two years later she was readmitted with an enlarged right inguinal gland. Her general health was good, her liver and spleen were not palpable, and an X-ray of her chest was clear. Bilateral inguinal dissection was performed, and section showed that two glands contained tumour cells similar to those of the primary, except that pigment

was now even less evident. Deep X-ray therapy was directed at the pelvis and inguinal regions. In November 1944 a nodule appeared in the breast, which biopsy proved to be of the same nature, and then further deposits appeared in the liver and bones, and the patient died in January 1945, three and a half years after the original operation.

Comment.—Vulval melanomata are very much rarer than the extensive literature suggests. Up to 1920 Kehrer found 83 case reports, and only 15 later records can be discovered.

The present case is remarkable in two respects: the youth of the patient, and that she was pregnant. In Holland's series (1908) the age was recorded in 33 cases, and 24 of these were over 50 years of age, and no patient was under 30. The average age in Kehrer's series was 54. It is exceptional to encounter a case in the twenties, although Sahler (1927) reported a case aged 28, and Curtis (1933) one aged 29. The latter was practically identical with the present case, and was a primigravida in the last month of her pregnancy, who had a pedunculated mole 1.5 cm. in diameter on one labium majus. This was excised at the time of delivery, and just as in the present case the report that it was a melanoma came as a surprise. Radium was applied to the tumour site and there was no recurrence in five years.

Hirst (1905) described a hyperacute case in a pregnant woman; who died four weeks after the melanoma was first noticed, and Labhardt (1924) and Naviatil (1936) stress the danger of pregnancy in patients with pigmented vulval moles, being of the opinion that pregnancy may stimulate a previously quiescent mole to activity.

In the present case the tumour had been present for some years. Although Holland stated that it is unusual for malignant melanomata to arise from a preceding mole this is certainly not the general opinion, and it would be counter to experience with melanomata arising in other sites; and indeed Gosforth (1926) stresses the danger of minor and incomplete interference with vulval moles.

Although the prognosis with a malignant vulval melanoma is almost hopeless (e.g. Holland reported only one three-year survival among 26 cases) there have been a few reported cures even after repeated partial operations (Meyer, 1907; Fischer, 1881). At Radiumhemmet (Schnagel, 1933) the treatment chosen was diathermy excision combined with X-ray radiation or telerradiation, with one three-year survival out of 4 cases.

It must be admitted that the full menace of this tumour that appeared relatively benign and was of long standing, was not at first realized, and the case strongly emphasizes the danger of all such tumours, particularly in pregnancy.

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Ovarian Cyst with Twisted Omental Pedicle.—F. H. FINLAISON, F.R.C.S., M.R.C.O.G.

Mrs. M. W., aged 39, was seen in the autumn of 1945 and complained of intermittent attacks of abdominal pain for the previous ten years. The pains were sharp in character and lasted up to an hour, occurring every two or three weeks. On examination a mobile cystic tumour about 7 in. in diameter was felt in the abdomen. It was slightly tender.

A diagnosis of ovarian tumour with intermittent torsion was made, and laparotomy was performed on October 10, 1945.

Operation: On opening the abdomen the tumour was easily withdrawn, and was found to be attached only to the great omentum, from which it obtained its entire blood supply, and which was twisted through two complete circles. The cyst had come from the right side and the stump of the fallopian tube was still attached to the uterus, but the infundibulo-pelvic ligament had disappeared. The pelvis was quite free from adhesions. The tumour itself was removed by cutting the omentum, and attached to it was the fimbrial end of the fallopian tube with a hydatid of Morgagni. Blood-vessels ran from the omentum to the cyst wall. It appeared to be a dermoid.

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menopause—are naturally more marked, for at those periods of life there is little or no oestrogenic hormone in the blood.

(2) This case is one of the rare examples of this group of tumours where the malignancy of the tumour is confirmed by clinical findings. It is not possible to diagnose malignancy (in the absence of invasive characteristics) on histological grounds alone. The general impression that granulosa-cell tumours are, in the main, benign, or at most, only locally malignant would appear to be too optimistic. Novak prefers to speak of the tumours not as granulosa-cell tumours but as granulosa-cell carcinomas. He has reviewed a series of 32 cases, and in the follow-up there was a clinical malignancy rate of 28.1%. (Novak & Brauner (1934) *Amer. J. Obstet. Gynec.*, 28, 637).

(3) Some patients do extremely well following upon operation. As it seems likely that there are grades of malignancy in granulosa-cell carcinomas their radical removal should be undertaken even in those cases where the prognosis may seem clinically hopeless.

Myxosarcoma of the Broad Ligament.—E. FRIEDMAN, M.D.

Patient, aged 35, has had one stillborn baby and regular normal periods, except for the last two or three which have been heavier.

Three months ago she noticed enlargement of her abdomen and complained of some frequency and pain in front of the left thigh on lying down. She also had a dry cough. Her general condition, however, was quite good. There was no loss of weight.

On examination a mass arising out of the pelvis was found, irregular, firm, the size of a baby's head and not mobile. The cervix was small and pushed high in the right fornix by a mass in the posterior and left fornix, which appeared to be part of the abdominal tumour. The uterus could not be felt. A provisional diagnosis of intraligamentous fibroids was made.

Operation.—When the abdomen was opened, a mass was found lying in the left broad ligament, immobile and firmly fixed to the bladder, colon and rectum. The uterus, ovaries and both tubes appeared to be normal. Any attempt to remove the tumour would have seriously endangered the patient's life. On section the tumour exuded a glairy mucinous fluid.

Microscopically it was a malignant tumour showing considerable myxomatous degeneration; it was of primitive fibre-forming connective tissue cells.

Comment.—Sarcoma of the broad ligament is rare in the English literature until 1936; the German literature had reported 55 cases up to 1914. Many more have been reported since from the Continent and from the United States.

Although sarcoma can occur in almost any part of the body, those of the broad ligament represent the smallest group. They occur either as a primary tumour, or as a sarcomatous degeneration of a true myoma of the broad ligament. They may also be metastatic. The primary sarcoma, i.e. that which springs from the connective tissue of the broad ligament, is said to be more frequent, more malignant and to give rise to metastasis more rapidly than a secondary sarcomatous growth. It also grows more rapidly.

Histologically it derives from an undifferentiated embryonic tissue which is believed to commence to grow under the stimulus of an impulse such as puberty, trauma or the menopause.

The tumour does not cause typical symptoms so that it can be mistaken for a fibroid, ovarian cyst or a tumour of inflammatory nature. The length of time the tumour has existed before treatment in reported cases varies from one to several years; they are usually found between the ages of 40 and 60.

Treatment.—Deep X-ray therapy might be worth a trial, especially in early cases with no metastases, but the prognosis is bad, even when the tumour has been entirely removed.

Suprarenal Hæmorrhage Complicating the Puerperium.—LOIS E. HURTER, M.B., B.S.

This patient died suddenly of acute bilateral suprarenal hæmorrhage on the 8th day of the puerperium, the cause of the hæmorrhage being obscure.

Case report.—Mrs. W., gravida 2, aged 33, was admitted to hospital on 28.11.45 in the 1st stage of labour. Her previous pregnancy, labour and puerperium had been quite

Recovery was uneventful, and on further questioning the patient recollected that at the beginning of the trouble ten years previously she had been attacked by severe abdominal pain which had persisted for two days.

It would appear that at this time complete torsion of the pedicle had been followed by sloughing of the cyst, but it had acquired a secondary omental attachment and blood supply. The omental pedicle in its turn had undergone intermittent torsion during the ensuing ten years, this accounting for the recurring milder attacks of abdominal pain.

Malignant Granulosa-Cell Tumour.—WILLIAM HAWKSWORTH, F.R.C.S.

Married woman, aged 38, first seen at the Radcliffe Department of Gynæcology, Oxford, on September 11, 1942.

She complained of having a constant desire to open bowels for past six months. Actually passes a motion two to three times a day. No blood or mucus in stools.

Menstrual history.—Menarche, aged 14. Katamenses—3/28; not excessive. Slight hypogastric pain first day of period. L.M.P. 19.8.42.

On examination.—Abdomen: N.A.D. Anal sphincter normal. Vaginal examination: Some laxity of the vaginal walls and introitus, but no cystocele or rectocele. Perineum firm.

Cervix healthy; uterus, anteverted but not enlarged; fornices, clear.

On January 14, 1944 (sixteen months after her first attendance) she reported again with complaint of severe stress incontinence which had been present for three months. Examination now revealed a mass arising out of the pelvis, palpable at the upper border of the symphysis. On bimanual examination this mass was considered to be uterine and probably due to the presence of fibroids. Vaginally there was some vault prolapse associated with cystocele and rectocele.

Operation.—Vaginal hysterectomy revealed a solid ovarian tumour firmly attached to the right lateral wall. The uterus was small and contained one or two seedling fibroids. The vaginal hysterectomy and posterior colpo-perineorrhaphy were completed and then the abdomen was opened. The right ovary was found to be replaced by a fungating mass which had spread laterally to the pelvic wall—this mass was separated with some difficulty from the ureter and iliac vessels and the clearing of the pelvis completed by bilateral salpingo-oophorectomy. Another neoplasm was found involving the terminal ileum about 9 in. from the ileo-caecal valve. The growth in the ileum was resected and an ileo-transverse anastomosis completed the operation. Convalescence was uneventful.

Follow-up: Subsequent examinations, the last being on May 3 of this year, i.e. two years and three months after her operation, have shown this patient to be in excellent health with no evidence of recurrence.

Histology.—The section of the right ovary showed sheets of cells of fairly uniform size with large nuclei. These sheets of cells are arranged more or less into islets, which are separated by small areas of connective tissue. Within the islets themselves there are numerous small spaces in which in some cases can be seen a degenerate nucleus and under a higher power a radial arrangement of cells round these spaces can be identified. These spaces are the typical Call-Exner bodies, and the arrangement of the cells into these islets gives rise to the so-called folliculoid type of this tumour. An identical histological appearance was reproduced in the other ovary and in the deposit in the terminal ileum. In view of these histological features and the way this tumour has spread there can be no doubt that this is a granulosa-cell carcinoma.

Summary.—(1) The characteristic symptomatology of granulosa-cell tumours is well known and although some disturbance of the menstrual rhythm is expected during the reproductive years, this is not always so, as in this case. It has to be remembered that the tumour adds quantitatively to the amount of circulating oestrogenic hormone in the blood, so that during the period of active adult sexual life the hyperoestrinism may be associated with hypermenorrhœa, amenorrhœa, or even with normal menstruation. The changes resulting from the addition of œstrin in the years before puberty or after the

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The essential features of the post-mortem report were a yellowish pallor to the skin, but the conjunctivæ were clear. There was a small hæmorrhage beneath lower end of sternum. The upper air passages were congested, there was old tuberculous scarring at the right apex and chronic emphysema of the upper lobes of both lungs. There were patchy areas of hæmorrhage in the right lower lobe. There was no pathological change in the cardiovascular system; in the alimentary system there was an area of hæmorrhage the size of a five-shilling piece into the mucosa of the cardiac end of the stomach and there were small areas of hæmorrhages into the mesenteric attachment of the jejunum. The liver weighed 1,720 grammes. The surface was mottled, there were small hæmorrhages beneath the capsule on the inferior surface. The pattern was coarse and some excess fat was present. The gall-bladder and biliary passages were normal.

The kidneys were pale, the pyramids congested and cortices pale. The pelvis on each side was dilated and congested and there were small hæmorrhages into the pelvis. The right ureter was slightly dilated. The bladder was normal and contained approximately 6 oz. of turbid pale urine. The uterus was well contracted and small subperitoneal fibroids were present. There were small portions of fibrinous clot adherent to lining of uterus. The ovaries were normal with a corpus luteum present in right ovary. The pelvic veins were healthy.

Brain, thyroid gland and pituitary gland appeared normal.

Both suprarenal glands were enlarged, the left weighed 55 grammes and the right weighed 75 grammes (normal weight 5 to 6 grammes). There was hæmorrhage into medullary portions of both glands, the cortices were stretched and thinned.

Histologically the heart muscles showed cloudy swelling, the liver cells were swollen, but there was no evidence of necrosis. The kidneys showed cloudy swelling of the tubule cells.

The suprarenals showed massive hæmorrhage into the medullary portion of the glands extending into and between the cells of the cortex. There was no evidence of thrombosis of the suprarenal vessels.

Comment.—Very few cases of hæmorrhage into the suprarenals in adults have been reported and of these only three have been associated with pregnancy. Hall & Hemkem reported a case in 1936 where there was hæmorrhagic infarction of the suprarenal due to thrombosis of the suprarenal vein in a patient with hyperemesis gravidarum. Keele & Keele in 1942 described a case also due to thrombosis of the suprarenal vein in a patient who had reached the 7th month of pregnancy. The third case, that of massive bilateral suprarenal hæmorrhage associated with necrosis of the liver during the puerperium, was described by Gladys Dodds in 1945.

It appears that the causes of hæmorrhage into the suprarenals are: Acute infective conditions, a general hæmorrhagic state, and in the newborn where there is the possibility of trauma and toxins playing a part.

This case is clinically more like those occurring in acute infections, but there was no evidence of any such infection in life or at the post-mortem examination.

The striking features are the associated small hæmorrhages with a possibility of a general hæmorrhagic state and the presence of shock which has been specifically excluded in other records. A transfusion reaction due to pyrogens has been considered and thought unlikely as no other such reaction occurred although the same citrate solution and same methods of storage had been used for blood given to other patients about the same time.

I should like to thank Miss Gladys Hill for allowing me to report the case.

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Pelvic Leiomyosarcoma.—BRAITHWAITE RICKFORD, M.D., F.R.C.S., M.R.C.O.G.

History.—Sister G., unmarried, aged 47, was complaining of an abdominal tumour reaching to the level of the umbilicus. This had been noticed for four months but there were no other symptoms.

On examination.—A smooth firmish doughy tumour was found, reaching to the umbilicus; and on bimanual examination, was thought to be ovarian in origin. A severe uterine hæmorrhage followed admission necessitating a curettage and transfusion. Microscopically the tissue removed was normal post-menstrual endometrium. A month later laparotomy was performed owing to severe abdominal pain. The peritoneal cavity contained a quantity of darkly stained hæmorrhagic fluid and a smooth walled elastic pinkish tumour arising to the level of the umbilicus. In several areas growing

normal and there was no history of any previous illness or operation. Antenatal care had been carried out at the hospital clinic, there had been no oedema, albuminuria or hypertension, the highest recorded blood-pressure being 125/85. Labour progressed normally, a full term, living, male child, weight 8 lb. 6 oz. being delivered spontaneously after twelve and a half hours. During the third stage of labour the patient had a post-partum hæmorrhage of 40 oz. for which no cause was found. The uterus contracted well following the administration of pitocin, 5 units. The general condition was good, the pulse-rate 88 and of good volume. She was given a warm drink and left to rest. Four hours after delivery the patient suddenly became severely shocked, the pulse was rapid and of poor volume, the blood-pressure fell. There was no further bleeding and she did not complain of pain. She responded well to warmth and the administration of two pints of directly compatible group 0 blood, the first pint being run in in one hour and the second pint over a period of three hours. (Group 0 blood was used as Group A was not readily obtainable on that occasion.)

The puerperium was uneventful for seven days apart from mild bronchitis and a moderately severe anæmia; Hb 58%. The uterus involuted well, the patient was apyrexial, the lochia normal and the bowels were open regularly. On the 8th day of the puerperium it was decided to give a further blood transfusion as the anæmia had not responded to iron therapy. A pint of directly compatible macroscopically and microscopically (checked by three observers) group A blood was selected and the transfusion started at 6 p.m. on 5.12.45. At 7.45 p.m. after approximately 5 oz. had run in, the patient complained of acute pain beneath the lower end of the sternum and in both loins; she vomited copiously and was suddenly incontinent of urine and feces. She became cyanosed and collapsed, the pulse was 140 and thready. The blood transfusion was immediately stopped and a sample of the donor's blood saved for repeating compatibility tests.

The diagnosis lay between "incompatible blood transfusion" and "pulmonary embolism".

On examination the patient was restless, cyanosed, breathing was laboured, she lay curled up in bed and resented interference. The chest was clear, the upper abdomen was tender, there was no tenderness in the loins as by this time the loin pain had passed off. Continuous oxygen was given by nasal catheter and finally by a B.L.B. mask. Warmth was applied and an intramuscular injection of 2 c.c. coramine was given. By 9 p.m. the general condition had greatly improved, the colour was good, the pulse below 100 and of better volume, the patient complained of no pain.

As the most likely diagnosis seemed to be incompatibility of the transfused blood, fluids were pressed by mouth and hot packs were applied to the loin, 60 grains of potassium citrate with 30 grains of sodium bicarbonate were given by mouth 2-hourly. By 10 p.m. the pulse had risen again to 130, but as the temperature was 104° this was thought to be reactionary. The patient was restless so morphia grain $\frac{1}{4}$ was given subcutaneously. The patient vomited twice more before midnight, 8 oz. and 6 oz., and one vomit was slightly blood-stained. She had been taking fluids well and appeared thirsty. A Ryle's tube was passed to save the patient the effort of vomiting and was aspirated hourly. An intravenous 5% glucose saline drip was commenced. The colour remained good and apart from restlessness her condition was satisfactory, the pulse remaining about 130. 2 drms. of paraldehyde were given intramuscularly. At 8 a.m. next morning, 6.12.45, the patient suddenly collapsed again and the pulse rose to 160, there was air hunger and she became cyanosed and breathless. By daylight it was possible to see that the skin had a yellowish tinge and the patient appeared dehydrated, though her intake had exceeded her output by 2 pints during the night.

2 c.c. coramine were given, continuous oxygen and 10 minims of 1:1000 adrenalin intravenously. The intravenous drip was changed to 4.285 normal sodium sulphate solution. On examination the patient was profoundly shocked, blood-pressure 40/20, but complaining of no pain. The chest was still clear. A further 2 c.c. of coramine was given intravenously. She rapidly lost consciousness, became comatose and died at 9.45 a.m. 6.12.45 despite all efforts at artificial respiration.

Post-mortem findings.—The compatibility of the donor's cells with the patient's serum and the donor's serum with the patient's cells was repeated and they were found to be directly compatible, macroscopically and microscopically. Death was found to be due to acute adrenal insufficiency caused by acute hæmorrhage into both suprarenals. There was no sign of blood incompatibility or of pulmonary embolism.

Section for the Study of Disease in Children

President—Professor NORMAN B. CAPON, M.D.

[March 22, 1946]

MEETING HELD AT GREAT ORMOND STREET HOSPITAL, LONDON

Hypoproteinaemia.—R. MEYER, M.B., M.R.C.P., for BERNARD SCHLESINGER, M.D., F.R.C.P.

Jean C., aged 3 years. Admitted 14.1.46. *Complaint:* Three weeks swelling of legs and abdomen. Two weeks coryza, loss of appetite, thirst and yellow diarrhoea.

Previous history.—Fit except for pneumonia one year ago and frequent colds.

Diet: Milk one pint daily. Meat once daily. Loves bread, sugar, cereals.

Family history.—Mother, father and 8 siblings alive and well. No complaints.

On examination (14.1.46).—Plump, pink child. Weight 31 lb. Coryza. Large tonsils. Gross oedema of legs, face and trunk. Ascites. Liver—2 fingerbreadths palpable—firm, not tender. No other abnormality including no skin, mucosal, or nerve lesions.

Investigations: Stools yellow and loose. No pathogens. No T.B. Fats: 29.7% dried faeces, 73.8% split. Urine n.a.d. Blood urea 21 mg./100 c.c. Kahn negative.

X-ray: Sinuses clear. Wrists, no abnormality. Chest: heart normal. Small right pleural effusion.

Plasma proteins: 2.55%, alb. 1.82%, glob. 0.73%.

Course: After six days on a light diet without improvement on 20.1.46 she was given thiamine intramuscularly 10 mg. daily for five days and Beminal 1 tab. b.d. by mouth. Oedema lessened the following day and had gone by 22.1.46. Weight dropped 5 lb. in two days and then rose to 27 lb. Liver remained palpable. She was happy and ate well. Discharged 2.2.46 on Beminal 1 tab. t.d.s. and normal diet.

Further investigations.—

	Serum protein	Alb.	Glob.
21.1.46: Takata-ara negative.			
Alk. serum phosph. 6 units.	14.1.46: 2.55%	1.82%	0.73%
24.1.46: Blood urea 23 mg./100 c.c.	21.1.46: 3.96%	—	—
30.1.46: Stool fat 26.3% dried faeces.	24.1.46: 4.54%	3.37%	1.17%
30.1.46: Dextrose tolerance normal.	2.2.46: 4.10%	3.02%	1.08%
30.1.46: Hb. 85% Sahli; W.B.C. 9,800.	22.3.46: 5.94%	3.75%	2.19%

Present weight 28 lb. Liver only just palpable. Symptoms: Coryza still, otherwise well, though restless at night. Impetigo one month ago. Has omitted Beminal tabs. for one month.

Dr. R. Bonham Carter: I would be glad of an explanation of the mechanism by which vitamin-B therapy has relieved the oedema in this case. Hypoproteinaemia, in the absence of renal disease, occurs, so far as I know, only in nutritional disorders in which failure of ingestion or absorption of protein is the cause. In such conditions vitamin-B deficiency might well be associated with hypoproteinaemia but is not necessarily the cause of it.

In about 200 cases of "famine oedema" seen at one P.O.W. camp in Germany no case could be said to have improved by vitamin-B therapy of a massive "blunderbuss" kind. On the other hand mild or early cases improved with rest in bed alone. Most of the prisoners of war had frequency which was directly related to their oedema—that is they were more oedematous when they had less frequency. Nocturnal frequency in these cases could, in part, be controlled by giving an evening meal of relatively high protein

through the tumour wall were thick fleshy exuberances which resembled organized blood clot, being a buffy colour near the tumour and a deep reddish brown at the periphery. The growth was firmly impacted in the pelvis and considered to be malignant. Removal was completed with considerable difficulty and on account of the amount of blood loss pan-hysterectomy was not attempted. The uterus, though adherent to the growth, was not apparently the origin of the tumour. The specimen was largely necrotic in the centre, containing much old blood; in other areas it was pinkish in colour, rather homogeneous in texture and with little if any architecture. A section taken from the most preserved area was reported to be a "fibromyoma with inflammation and necrosis". In view of this radiotherapy was not considered to be indicated.

Five months later a recurrence was present, causing obstruction of the pelvic colon. A colostomy was carried out. A tumour similar to the first was arising from the pelvis and there were large soft pinkish white fleshy secondaries growing over the peritoneum. One of these about $2\frac{1}{2}$ in. high and $\frac{1}{2}$ in. thick was growing at the fundus of the bladder. Its appearance was arresting. The surface of this growth was undergoing rapid fibrillary contractions, corrugating into grooves, resembling the surface of a post-partum uterus, and the whole mass was generally contracting and relaxing like the movements of a jelly-fish, but at a much more rapid rate.

A biopsy was taken from here which was reported to be a "spindle cell sarcoma". The patient died two months later, a post-mortem was performed, and a search was made to elucidate the cause of the twitching of the secondaries. All areas of metastasis were examined microscopically and in a section from a pleural growth unstriated muscle was demonstrated.

The point of interest in this case is the presence of motility in an apparently spindle-celled sarcoma, and the presence of unstriated muscle cells among an area of spindle-celled sarcoma in a distant metastasis, giving strong evidence in support of Handley & Howkins' contention that uterine sarcoma originating in a fibroid always grows from the muscle cells.

REFERENCE

HANDLEY, R. S., and HOWKINS, J. (1937) *Lancet* (ii), 1180, 1246.

Treatment.—She is receiving 15 grains of pancreatin (enteric coated) with each meal. 60 grains a day. Normal diet with no restriction of fat. Vitamin supplements, particularly vitamin-A.

Progress: Her weight gain has been satisfactory since starting pancreatin, she now appears well-nourished though still undersized. However, she is still very susceptible to respiratory infections.

Fibrocystic Disease of the Pancreas.—R. J. PUGH for BERNARD SCHLESINGER, M.D., F.R.C.P.

Female infant, aged 10 months. An only child, born after a normal labour, weighing 7 lb. and completely breast-fed for five months. subsequently partially until weaning was complete at eight months. The patient took her feeds extremely well, never vomited but from birth passed poorly-formed creamy stools, usually twice in the twenty-four hours. These were markedly offensive and exhibited a rancid smell on standing. Since the age of 6 months when the weight reach 14½ lb. there had been no further gain and the stools are said to be "in a yellow oil, passed liquid but solidifying in the pot." For the last three weeks there has been a persistent cough.

Findings: An underweight infant, 14 lb. 5 oz. at 10 months with a good colour, normal contours and no abnormalities to be found on examination.

Stool: Total fat 42.7% of dry weight, 34.4% of which is split. The stool shows excess of undigested and partially digested starch, undigested meat fibres and a slight excess of small fat droplets (Dr. W. W. Payne).

Fat absorption: On a 30 gramme daily dietary, 10.01 grammes fat were lost daily in the stools.

Duodenal enzymes effect no digestion of gelatin up to a 1:3 dilution.

X-ray Chest: Lung fields appear clear.

Treatment.—Mixed dietary to match appetite with pancreatin, grains 60, daily, given in four divided doses a.c. and halibut liver oil mxxv b.d.

Mongol with Abscess in Neck from Tuberculosis of Cervical Spines.—D. ELKIN, M.B., Ch.B., for CHARLES DONALD, O.B.E., F.R.C.S.

M. L., aged 2½ years.

History.—Lump in neck, first noticed by the mother 2½ months ago, steadily increased in size. Child has lost weight over the past six months.

On examination.—Classical mongoloid appearance, bilateral nystagmus. Rounded fluctuant mass in the posterior cervical region, lying under the skin and apparently attached to bone. Full movement in the spine, etc.

Investigations.—Aspirated pus: Thick, creamy, no tubercle bacilli. Mantoux reaction: 1/1,000 positive. X-ray: Pott's disease. Chest normal. C.S.F. normal.

Conclusion: Cervical Pott's disease originating from the spinous processes.

Von Gierke's Disease.—D. ELKIN, M.B., Ch.B., for T. TWISTINGTON HIGGINS, O.B.E., F.R.C.S.

J. B., aged 2 years. Complaint: Swelling of the abdomen, first noticed six months ago, at a time when the child was wasted after pertussis. It increased rapidly at first, but has now seemed stationary for four to six weeks.

On examination.—General condition excellent. Liver grossly enlarged, with a smooth surface, regular outline and firm consistency. Spleen not palpable. Otherwise normal.

Investigations.—Urine and blood normal. Alk. serum phosphatase 14.8 units.

Adrenaline response	Fasting	¼ hr.	½ hr.	¾ hr.	1 hr.
22.2.46: Blood sugar	75	80	106	85	80
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Conclusion: Probably Von Gierke's disease.

After the meeting laparotomy was performed and revealed a smooth pale homogeneous liver. Biopsy confirmed the diagnosis.

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D. B., male, aged 7½ years, was admitted April 1945. Youngest of a family of four, the other members of which are healthy.

content. This pointed to a direct relationship between protein intake and water balance. Such a relationship has already been described. Lastly, established cases of "famine oedema" require rehabilitation on normal or high protein diet for some weeks before the oedema disappears, and it will reappear, if such men are subsequently subjected to a low protein diet, more quickly in them than in normal subjects upon the same deficient diet.

Rheumatoid Arthritis with Unusual Onset.—B. SCHLESINGER, M.D., F.R.C.P.

A boy aged 4 years was admitted to hospital acutely ill and in some distress. There was a history of a cold with earache three weeks previously, followed by vague joint pains. Acute pericarditis and pleurisy with a small effusion soon developed with high pyrexia. There was no degree of myocarditis other than slight changes in the E.C.G.'s. As his pericarditis subsided, superficial glandular enlargement appeared and typical rheumatoid changes became evident in several joints, particularly the ankles and cervical vertebræ.

Fibrocystic Disease of the Pancreas (Two Cases).—A. D. BARLOW, M.R.C.P., for DONALD PATERSON, F.R.C.P.

(1) Female, born 15.4.45.

History.—Birth-weight 4 lb. 8 oz. Full term. Very slow gain in weight until 6 months old, when she weighed 9 lb. She then developed a cough which persisted for two months increasing in severity till 8 months when she was admitted to Great Ormond Street with bronchopneumonia. Despite an adequate caloric intake she was very undersized. She had taken her feeds well, but her mother had noticed pale undigested stools with a rancid smell since birth.

On admission.—Weight 7 lb. 12 oz. She was cyanosed and dehydrated and grossly emaciated. Moist râles were audible at both bases. Following treatment with penicillin her condition improved and she started to gain weight very slowly. On clinical grounds diagnosis of fibrocystic disease of the pancreas was considered and this was confirmed by the investigations.

Investigations.—Chest X-ray: There is collapse and patchy consolidation in the mid and lower zones of both lungs. Blood-count normal. Stool fats: Total 28.8% of dry faeces. Split fat 19.2%. Duodenal juice: Failure to digest gelatin on two occasions. Serum protein: 5.8 grammes per 100 c.c.

Treatment.—Child was given peptolac (Cow and Gate) with added Savory and Moore's Food. Pancreatin grains 15 was given with each feed.

Apart from a small gain in weight when first admitted her progress has been highly unsatisfactory.

Since the meeting the child has died. Post-mortem confirmed the diagnosis; section of the pancreas showing increased fibrosis and dilatation of the ducts.

(2) G. B., female, born 18.1.40.

History.—Frequent upper respiratory infections since 3 months old. Very poor weight gain. Large abdomen, and large pale offensive motions since 1 year old. Her appetite had always been good.

She is the only child, and there is no relevant family history.

First admitted in June 1942 for intractable rectal prolapse, which was successfully treated by perianal injection of alcohol. At that time she was thought to be a case of coeliac disease. The stool fats were 40.5% (66% split), and contained an excess of undigested meat fibres and starch granules. However, she showed early clubbing, the liver was palpable nearly 1 inch below the costal margin, and an X-ray of her chest showed a mottling at both hila.

She was treated as a case of coeliac disease, but gained little weight.

On 20.5.44 she was readmitted, at 4 years old her weight being 25 lb. Investigations now revealed that she was a case of fibrocystic disease of the pancreas.

Investigations.—Mantoux 1:1,000 neg. Chest X-ray: Rather increased hilar shadows. Blood-sugar tolerance curve (oral): Fasting 84 mg., peak rise 21 mg. Vit. A absorption: Fasting 34 units; after test dose 32 units. Duodenal juice: Gross reduction in trypsin (digestion of gelatin only occurred at 1:6 dilution).

The diagnosis is suggested by the occurrence of persistent chest symptoms in a child showing the clinical picture of coeliac disease, and yet with a good appetite, and is confirmed by the almost complete absence of pancreatic trypsin from the duodenal juice.

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On examination.—Classical mongoloid appearance, bilateral nystagmus. Rounded fluctuant mass in the posterior cervical region, lying under the skin and apparently attached to bone. Full movement in the spine, etc.

Investigations.—Aspirated pus: Thick, creamy, no tubercle bacilli. Mantoux reaction: 1/1,000 positive. X-ray: Pott's disease. Chest normal. C.S.F. normal.

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Gaucher's Disease.—L. ROWLEY, M.B., for DONALD PATERSON, F.R.C.P.

D. B., male, aged $7\frac{1}{2}$ years, was admitted April 1945. Youngest of a family of four, the other members of which are healthy.

On examination.—Liver and spleen were found to be enlarged down to the level of his umbilicus, both were firm and hard and the liver surface was irregular. There was no evidence of ascites or portal obstruction and his general condition was good.

Splenectomy and liver biopsy were performed in May 1945. Sections were demonstrated.

	April '45.	Feb. '46.
Serum protein	5.4%	7.3%
Serum cholesterol (normal 100-220) ...	125 mg. %	140 mg. %
Alkaline serum phosphatase (5-15 units)	7.0 units	18.5 units
Prothrombin time (up to 30 secs.) ...	22 secs.	28 secs.
Takata-ara reaction	negative	positive
Blood-count: Red cells 4.9 millions; Hb. 90%; W.B.C. 9,800; polys. 68%; lymphos. 32%.		

He was reinvestigated in February, 1946 as in table above.

Since operation his liver has increased in size and has become more nodular.

Infantilism of Renal Origin.—L. ROWLEY, M.B., for DONALD PATERSON, F.R.C.P.

C. S., male, aged 1 year 7 months. Admitted in January 1946. Vomiting after meals on and off since birth.

He is an only child, born at full term after a normal pregnancy and delivery. His birth-weight was 4 lb. 1 oz. He was bottle fed with frequent changes in brands of dried milks. He was seen to be small for his age but of normal proportions and no abnormal physical signs were elicited.

Height 25 in. (average 30 in), weight 12 lb. (av. 23 lb.), chest 15½ in. (av. 18½ in.), head 17 in. (av. 18½ in.).

He was found to have an insatiable thirst and to be drinking an abnormally large amount of fluid. Routine urine examination showed 85 mg. % albumen.

Blood-count.—R.B.C. 5.3 millions; Hb. 90%; W.B.C. 10,900.

E.S.R. 28 mm. in one hour.

Blood W.R. and Kahn tests negative.

Blood Biochemistry: Serum calcium 9.9 mg. % (9 to 11); inorganic blood phosphorus 5.8 mg. % (4 to 5.5); alkaline plasma phosphatase 2.6 units (10 to 20); plasma proteins 5.31%, normal proportions; plasma bicarbonate 28.2 vols. CO_2 (53 to 77); plasma chlorides 701 mg. % (560 to 630) as NaCl.

Urine: Albumen 85 mg. %. No abnormal deposit.

Blood urea 96 mg. %.

Urea clearance test: (1) 26.1%. (2) 21.6%.

Excretion pyelogram: Dye not concentrated sufficiently to show on X-ray plates.

X-ray: Long bones thin and small, cupping of lower end of ulna; wrists normal ossifications.

Lateral Sinus Thrombosis due to Acute Mastoiditis: Recovery with Penicillin.—H. A. FRASER, for JAMES CROOKS, F.R.C.S.

The patient was a boy aged 7 years who was admitted on 4.3.46 with a history of right earache for one week with purulent otorrhoea for three days following spontaneous perforation of the drum. His mother had noticed a lump in his neck high up on the right side for one day prior to admission. The child had been unwell with lassitude and anorexia for several days but had not had a very high temperature. He had been given inadequate doses of sulphathiazole for four days before admission. There was a past history of recurrent attacks of otitis media since measles at the age of 3 years.

On admission he was an ill, flushed child, T. 103°F., P. 130. Acute right mastoiditis with an abscess about the size of a hen's egg in the neck below the tip of the mastoid process. He was very deaf indeed. Central nervous system normal.

At operation a right cortical mastoidectomy was performed, the lower portion of the lateral sinus being found to be collapsed and thrombosed with a peri-sinus abscess leading to the abscess in the neck. The sinus was not opened, nor ligated, but the wound was packed open with ribbon gauze and a tube inserted for instillation of penicillin, 3,000 units four-hourly. The child was also put on systemic penicillin 10,000 units four-hourly and sulphamezathine in full doses. A total of 161,000 units of penicillin was given locally, and systemic penicillin was continued for a fortnight, total 850,000 units.

The child has made an uninterrupted recovery after running an intermittent pyrexia for two days after the operation, without any sign of rigors or central nervous system involvement.

Influenzal Meningitis.—D. J. CONWAY, M.B., for DONALD PATERSON, F.R.C.P.

M. J., aged 1 year 1 month.

History.—21.2.46: Admitted as an emergency. Collapsed this morning at a Nursery School. Previously quite well. Temp. 100, P. 144. Toxic, slightly cyanosed, neck rigidity and Kernig sign positive. Other systems N.A.D.

C.S.F. turbid and cultured *H. influenza*, type B. Put on sulphadiazine, penicillin intramuscularly and intrathecally also *H. influenza*, type B. antiserum (rabbit) Squibb.

Lumbar puncture C.S.F. percentage	Sulphadiazine	Penicillin intramuscularly	Penicillin intrathecally	<i>H. influenza</i> antiserum
21.2.46: Turbid, protein 320 mg. sugar 52 mg. Chlorides: 680 mg. Cells: 1,283 W.B.C. 307 R.B.C./c.mm. Polys. 99, monos. 1 Culture: <i>H. influenza</i> type B (Pittman)	1 gramme 4-hrly.	8,000 units 4-hrly.	6,000 units	
23.2.46: Sulphadiazine level 6.6 mg.	Blood, 12.6 mg. %		5,000 units	20 mg. I.V.
25.2.46: Protein: 130 mg. Sugar: 66 mg. Chlorides: 690 mg. Cells: 87 W.B.C. 33 R.B.C./c.mm. Polys. 95 Culture: sterile Sulphadiazine: 6.2 mg.			3,000 units	12 mg. I.V.
27.2.46: Hazy, blood-stained Protein: 200 mg. Sugar: 74 mg. Cells: 26 W.B.C. 584 R.B.C./c.mm.			3,000 units	
1.3.46: Protein: 150 mg. Sugar: 34 mg. Cells: 63 W.B.C. 294 R.B.C./c.mm. Culture: sterile Sulphadiazine level 17.3 mg.		Stopped at 252,000 units	3,000 units	
4.3.46: Protein: 80 mg. Sugar: 42 mg. Cells: 21 W.B.C. 563 R.B.C. c.mm.	Stopped after 30 grammes		3,000 units	
7.3.46: Protein: 60 mg. Sugar: 58 mg. Cells: 9 W.B.C., 10 R.B.C.				

22.2.46: Greatly improved; neck rigidity almost nil. W.B.C. 15,200. Polys. 24%, lymphs. 68%.

4.3.46: Almost completely well. W.B.C. 6,000. Polys. 34%, lymphos. 62%, monos. 4%.

8.3.46: Discharged home.

Influenzal Meningitis.—D. J. CONWAY, M.B., for BERNARD SCHLESINGER, M.D.

R. H., aged 1 year 5 months.

History.—21.2.46: Taken ill, temperature raised. No physical signs.

1.3.46: Slight injection of right tympanic membrane. Started on a course of sulphamezathine 12½ grammes.

4.3.46: Right paracentesis; a little fluid blood only, temperature 102°-103°. No diarrhoea, vomiting, rashes or pyuria.

15.3.46: Admitted to Great Ormond Street. Pale miserable child. Positive physical signs; small nodular posterior cervical gland, neck rigidity present. Kernig sign negative, fundi normal; knee-jerks rather brisk and plantar responses equivocal.

Lumbar puncture: Turbid C.S.F. No increased pressure. Queckenstedt: no block. Cells 1,000/c.mm. Protein 120 mg.

Culture: *H. influenza* type B (Pittman).

17.3.46: I.V. infusion ½ strength Hartmann's solution with glucose 5% set up.

18.3.46: W.B.C. 27,000. Polys. 81%, lymphos. 19%.

21.3.46: Since admission his general condition has shown very little improvement. Neck rigidity remains. He lies quietly, whimpers when interfered with, eyes usually closed, takes his diet moderately well. Twitched right side of body for ½ minute. Temperature normal today.

- 22.3.46: Twitched right side of body for $\frac{1}{2}$ minute on two occasions. ? Encephalitis.
 23.3.46: Twitched right side of body for $\frac{1}{2}$ minute on six occasions. None after then.
 27.3.46: Sitting up and fairly happy.
 4.4.46: Well, though rather irritable.
 6.4.46: Discharged home.

Lumbar puncture percentage C.S.F.	Cisternal puncture C.S.F.	Sulphadiazine	Penicillin intramuscularly	Penicillin intrathecally	<i>H. influenzae</i> antiserum
16.3.46: Turbid. Cells: 1,000 c.m.m. Protein: 120 mg. Culture: <i>H. influenzae</i>		1.0 gramme stat. 0.5 gramme 4-hrly. orally	5,000 units	5,000 units 8 p.m.	
17.3.46: Cells: 2,100 c.m.m. Protein: 140 mg. Turbid	Cells: 870 Protein: 90 mg. % Turbid			5,000 units and 7,500 into cisterna	40 mg. antiserum (Squibb)
18.3.46: Cells: 2,834 W.B.C. 173 R.B.C. Culture: No growth Sugar absent Sulphadiazine level 3.0 mg.	Cells: 812 W.B.C. 234 R.B.C.			5,000 units	25 mg.
19.3.46: Cells: 2,600 W.B.C. Sugar: 21 mg. (blood-stained)		1 gramme 6-hrly. Given I.V.		5,000 units	25 mg.
20.3.46	Clear fluid Cells: 217 c.m. Sugar: 36 mg. % Sulphadiazine 3 mg. %			7,500 units into cisterna	20 mg.
21.3.46: Clear fluid Protein: 36 mg. Sulphadiazine level 9.6 mg. Cells: 156 W.B.C. 37 R.B.C. Sugar: 27 mg. Culture: No growth		Blood Sulphadiazine 11.8 mg. %		5,000 units	
23.3.46: Sugar: 26 mg. Cells: 44 W.B.C. 1,020 R.B.C.		0.5 gramme 6 hrly.		5,000 units	
25.3.46:		Total 28 grammes			
26.3.46: Sugar: 42 mg. Protein: 80 mg. Culture: No growth Cells: 24 W.B.C. 161 R.B.C.					
4.4.46: Clear C.S.F. Protein: 60 mg. Sugar: 52 mg. Cells: 6 W.B.C. 85 R.B.C. Culture: No growth					
				1.4.46 Total 470,500 units	

Comment.—*Haemophilus influenzae* meningitis is an uncommon disease carrying a high mortality rate particularly in those under 5 years of age. *H. influenzae* has been classified by Pittman into six pathogenic types A—F of which type B is most important. It has been shown that this organism has a halo and that in infections a soluble specific polysaccharide can be found in the body fluids and urine much as in pneumococcal infections. The capsular swelling technique forms one of the methods of diagnosis and the reverse method of testing the patients' serum against the organism will show the adequacy of antiserum treatment. The mode of onset of this variety of meningitis may be sudden or a vague illness may only develop meningeal signs after two to three weeks.

The treatment of *H. influenzae* meningitis combines the use of sulphadiazine and antiserum. The use of the two together shows much better results than either singly. Penicillin intramuscularly and intrathecally is now used as well, though the sensitivity of *H. influenzae* to penicillin is not great and very variable. The antiserum is made from rabbits as the molecules are considered to be smaller and thus pass into the C.S.F. more readily. The antiserum has not been used to any great extent in this country, because of shortage of supplies. Certain firms here are commencing its manufacture.

The C.S.F. in *H. influenzae* meningitis is similar to that in pneumococcal or meningococcal meningitis, i.e. turbid C.S.F. of high cell content, mainly polymorphs, decreased sugar and chlorides, and increased protein.

Dr. H. E. Alexander of New York (*Amer. J. Dis. Child.*, 1943, 66, 172), an authority on this type of meningitis, recommends that when all material necessary for determining the causative organism in a purulent meningitis has been obtained, sulphadiazine should be started intravenously.

When *H. influenzae* Type B is isolated an intravenous drip is put up and in the next four hours more sulphadiazine is given and a large quantity of fluid (40 c.c. per kilogram body-weight) in an attempt to speed up urinary excretion of specific soluble substance. During the next two hours the dose of antiserum diluted with Ringer's or physiological saline equivalent to 10 c.c. per kilogram is given by the drip.

The level of C.S.F. sugar before treatment reflects the severity of infection and the dosage of antibody is recommended on the basis: Less than 15 mg. requires 100 mg. of antiserum (estimated as antibody nitrogen), 15 to 25 mg. sugar requires 75 mg., 25 to 40 mg. sugar requires 50 mg. and over 40 mg. sugar/100 c.c. requires 25 mg. of antibody nitrogen.

If after twelve hours the patient's serum does not produce capsular swelling of a suitable suspension of *H. influenzae* in a dilution of 1:10, an extra 25 mg. of antiserum is given and the serum is re-tested a few hours later.

If within twenty-four hours no organisms are seen in the C.S.F., the chlorides and sugar levels have risen, and there is adequate antibody as tested by capsular swelling, no more antibody need be given. If after forty-eight hours satisfactory progress is lacking a dose of antiserum equivalent to 25 mg. of nitrogen is given intrathecally.

The parenteral sulphadiazine in the first twenty-four hours should maintain a blood level of 15 mg. per 100 c.c. Then if the patient appears better 0.1 gramme/kilogram sulphadiazine is administered by mouth up to seven days after the C.S.F. is first shown to be sterile.

Thymoma.—N. F. E. BURROWS, B.M., for W. G. WYLLIE, M.D.

D. L., male, aged 3 months.

A case of a full term, normal labour, breast fed baby. Three weeks ago he started losing weight and vomiting. Stools were constipated, but later became green and slimy. The doctor who was called to see him was unable to palpate the heart apex and found stony dullness over almost the entire anterior chest wall.

He was admitted to Great Ormond Street Hospital on 9.12.44, where these findings were confirmed, and X-ray with barium swallow revealed that the œsophagus was displaced backward by a mass situated anteriorly in the mediastinum, thought to be a tumour of thymic tissue or of nerve tissue origin.

He was given a course of diagnostic X-rays by Dr. Hilton at University College Hospital but this made very little appreciable difference to the size of the tumour. Accordingly, it was considered likely to be of a benign nature, and operation was undertaken by Mr. Denis Browne. A large tumour weighting 350 grammes was removed, which on section proved to be a thymoma.

Convalescence was uneventful, and when last seen (March 1946) he was normal in all respects.

Myasthenia Gravis (Two Cases).—N. F. E. BURROWS, B.M., for W. G. WYLLIE, M.D.

(1) P. N., female, born 9.7.41.

History.—Quite well till October 1944 (aged 3 years) when she developed left ptosis.

Three months later ptosis became bilateral.

Five months after this (June 1945) the left side of her mouth was seen to be drooping, and her face became expressionless. In August 1945 she started tripping easily and fell several times. One day she collapsed and attempted to cough up a lot of phlegm. She became tired very easily, but after an hour's rest symptoms of tiredness and weakness abated somewhat.

Examination and treatment.—She was admitted to Great Ormond Street Hospital on October 17, 1945, as an emergency. She was white, collapsed. Her breathing was almost solely diaphragmatic, and her entire chest was full of moist sounds.

She was given 0.25 mg. prostigmin and 1/150 grain atropine subcutaneously, and in five minutes her breathing deepened, and she made attempts to cough. Ocular movements were restricted to fixed or central vision. She was hardly able to swallow. Pupils large. Reaction to light practically nil (possibly due to atropine). Facial movements weak. Knee-jerks equal and brisk. Arm-jerks brisk, and plantars flexor. Next day she collapsed again in a similar fashion. She became very cyanosed, and after being given 0.5 mg. prostigmin she was put in the Drinker respirator, and tube fed.

- 22.3.46: Twitched right side of body for $\frac{1}{2}$ minute on two occasions. ? Encephalitis.
 23.3.46: Twitched right side of body for $\frac{1}{2}$ minute on six occasions. None after then.
 27.3.46: Sitting up and fairly happy.
 4.4.46: Well, though rather irritable.
 6.4.46: Discharged home.

Lumbar puncture percentage C.S.F.	Cisternal puncture C.S.F.	Sulphadiazine	Penicillin intramuscularly	Penicillin intrathecally	<i>H. influenzae</i> antiserum
16.3.46: Turbid. Cells: 1,000 c.mm. Protein: 120 mg. Culture: <i>H. influenzae</i>		1.0 gramme stat. 0.5 gramme 4-hrly. orally	5,000 units	5,000 units 8 p.m.	
17.3.46: Cells: 2,100 c.mm. Protein: 140 mg. Turbid	Cells: 870 Protein: 90 mg. % Turbid			5,000 units and 7,500 into cisterna	40 mg. antiserum (Squibb)
18.3.46: Cells: 2,834 W.B.C. 173 R.B.C. Culture: No growth Sugar absent Sulphadiazine level 3.0 mg.	Cells: 812 W.B.C. 234 R.B.C.			5,000 units	25 mg.
19.3.46: Cells: 2,600 W.B.C. Sugar: 21 mg. (blood-stained)		1 gramme 6-hrly. Given I.V.		5,000 units	25 mg.
20.3.46	Clear fluid Cells: 217 c.m. Sugar: 36 mg. % Sulphadiazine 3 mg. %			7,500 units into cisterna	20 mg.
21.3.46: Clear fluid Protein: 36 mg. Sulphadiazine level 9.6 mg. Cells: 156 W.B.C. 37 R.B.C. Sugar: 27 mg. Culture: No growth		Blood Sulphadiazine 11.8 mg. %		5,000 units	
23.3.46: Sugar: 26 mg. Cells: 44 W.B.C. 1,020 R.B.C.		0.5 gramme 6 hrly.		5,000 units	
25.3.46:		Total 28 grammes			
26.3.46: Sugar: 42 mg. Protein: 80 mg. Culture: No growth Cells: 24 W.B.C. 161 R.B.C.					
4.4.46: Clear C.S.F. Protein: 60 mg. Sugar: 52 mg. Cells: 6 W.B.C. 85 R.B.C. Culture: No growth					
				1.4.46 Total 476,500 units	

Comment.—*Haemophilus influenzae* meningitis is an uncommon disease carrying a high mortality rate particularly in those under 5 years of age. *H. influenzae* has been classified by Pittman into six pathogenic types A–F of which type B is most important. It has been shown that this organism has a halo and that in infections a soluble specific polysaccharide can be found in the body fluids and urine much as in pneumococcal infections. The capsular swelling technique forms one of the methods of diagnosis and the reverse method of testing the patients' serum against the organism will show the adequacy of antiserum treatment. The mode of onset of this variety of meningitis may be sudden or a vague illness may only develop meningeal signs after two to three weeks.

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Breathing: Really good clearing cough, which was not possible a few minutes before.

After half an hour she was eating with a spoon a large plate of greens, potatoes and meat, and was able to stand by herself (*see figs.*).

Five hours later the effect of the prostigmin had worn off and she was unable to swallow, had almost complete ophthalmoplegia, and was becoming more expressionless.

A further similar injection was given, and in fifteen minutes she was able to finish her supper without trouble.



FIG. 1.—Before prostigmin.



FIG. 2.—Ten minutes after 0.25 mg. prostigmin.



FIG. 3.—Twenty minutes after 0.25 mg. prostigmin.

A few days later she was given prostigmin orally, 10 mg. four-hourly, later increased to three-hourly, as the effect had waned by the time her next dose was due.

On 5.2.46 Mr. Geoffrey Keynes removed her thymus. Pre-operatively she was given 0.3 mg. prostigmin subcutaneously and post-operatively 0.25 mg.

After a few stormy days post-operatively, she improved, and her dose of prostigmin was reduced from 15 mg. three-hourly to nil. Without any prostigmin she was not so lively and her ptosis was marked, although her general condition was excellent. She was put on a maintenance dose of 5 mg. prostigmin five times a day, and has remained well on this.

The thymus on section was normal, and weighed 5.5 grammes.

Subacute Nephritis.—A. P. NORMAN, M.B., for DONALD PATERSON, F.R.C.P.

C. M., male, aged 5½ years, born 13.11.40.

Previous history and family history not relevant.

September 1945: Onset of fever, abdominal pain, vomiting; transient swelling of right elbow, wrist and right testicle. On admission, found to have oedema of the face, purpuric spots on the arms, and hæmaturia.

Urine: Addis count:

Vol. 50 c.c. in 12 hours.

Albumin 260 mg.

R.B.C. 2,200,000

W.B.C. 500,000

} in 24 hours.

Casts nil.

Blood-count.—Bleeding and coagulation time within normal limits.

Blood urea 36 mg./100 c.c.

October 1945: Purpuric spots still present: Melæna. Loud systolic apical murmur, and enlargement of the heart, child extremely ill. Later in the same month developed a right pleural effusion. Then gradual improvement was noticed, fall in temperature, diminution of hæmaturia.

Blood urea 128 mg./100 c.c. Plasma proteins 4.9%.

From January till March 1946 he was in bed at home.

March 1946: General condition good.

Urine: Addis count:

Vol. 340 c.c. in 12 hours.

Albumin 120 mg.

R.B.C. 1,054,000

W.B.C. 102,000

Casts 68,000

} in 24 hours.

B.S.R. 9 mm. in 1 hour.

Urea clearance 100% of normal.

Blood urea 38 mg. %.

Plasma proteins 5.74 grammes %.

Blood-pressure 120/80.

X-ray chest: Heart and lungs normal.

Investigations.—X-ray of thymus showed no evidence of enlargement.

Blood-count: R.B.C. 5,260,000; W.B.C. 26,100.

Progress: Prostigmin dose increased to 0.75 mg. six-hourly and atropine grains 1/150 subcutaneously, without any marked improvement in general condition. Later, one mg. prostigmin four-hourly was given, and her general condition suddenly improved.

On October 21, 1945, she was given 45 mg. prostigmin increased to 60 mg. orally q.d.s. This caused an increase in her chest expansion, but did not affect her ptosis or ocular movements.

She was given rests in the Drinker for a few hours each day until October 28, 1945, when it was discontinued. On October 25 the prostigmin was stopped for thirty hours, and at the end of that time, as her face had become more expressionless, it was restarted at 15 mg. t.d.s.

Prostigmin was stopped for a period of five days in early November, and the child's general condition was still good at the end of this time.

Operation.—On November 13, 1945, her thymus was removed. Prostigmin 1 mg. being given by injection before, and repeated after, operation.

On coming round from the anæsthetic her eyes were wide open and remained thus for four days, although her ocular movements were not full. Her ptosis returned four days later, by which time her dose of prostigmin had been reduced to 15 mg. six-hourly by mouth. A week later her eyes opened better, particularly in the mornings, and a few days after that they were wide open, although ocular movements were poor.

She was discharged from hospital 3.12.45, and has since reported monthly.

Her mother states her eyes are well open, and her ocular movements good in the early morning, but when last seen she had bilateral partial ptosis, and practically no ocular movements. Her general condition was excellent. After her last visit here she was put on prostigmin 5 mg. q.d.s.

The thymus on section was normal, and weighed 17 grammes.

(2) J. B., female, born 14.6.43.

History.—Full-time normal delivery. Birth-weight 7 lb. 15 oz. General condition satisfactory until four weeks before admission when she had drooping of the left lid and left facial weakness. Two weeks later she began to fall to the left when walking, had difficulty in swallowing, and her speech became nasal.

On examination.—Slight ptosis left eyelid and weakness left corner of mouth, with left palatal paralysis.

No wasting or loss of power in the limbs. Fundi normal. Pupils reacted to light and accommodation, but ocular movements restricted. No nystagmus. All reflexes present and normal.

Investigation.—C.S.F.: Clear colourless fluid. Protein: 20 mg.; Sugar: 96 mg.; Chloride: 730 mg.; Culture: Sterile. No cells.

Progress: She was thought to be a case of polyneuritis cranialis, and sent to Great Ormond Street Convalescent Home at Tadworth 22.10.45. Here she gradually improved over a fortnight, but suddenly had an acute central respiratory crisis in which she went black, and had to be given artificial respiration. She improved slightly with tipping, oxygen, strychnine and adrenalin. Her chest was extremely bubbly.

In three days she had got over this attack, but the following day she had another, only less severe.

For four weeks she was moderately well—her facial weakness was improving, she was swallowing more easily—until 28.12.45, when she became cyanosed, and brown fluid poured from her nose and mouth. Breathing became difficult and bubbly. Resuscitation methods tided her over this crisis for forty-eight hours, but her palatal paralysis then became more marked, and she had to be tube fed.

She was readmitted to Great Ormond Street 4.1.46 in poor condition—no intercostal movement, and clear stringy mucoid discharge pouring from her mouth and nose. All reflexes were present but inclined to be sluggish. No papilloedema. Pupils showed sluggish response to light.

Once again she was tipped, given oxygen and atropine. Next day she was improved, but ptosis was marked and her face was completely expressionless. She was able to hold the sides of the cot for a minute or so, and then her arms would flop down on to the bed. Still tube fed.

At this point she was given 0.25 mg. prostigmin and 1/150 grain atropine.

In ten minutes she was more lively, and in twenty minutes her picture was as follows—

Face: Return of expression, smiling with ease.

Eyes: Ptosis improved. Able to raise lids, and eyes able to move.

Deglutition: No signs of milk or saliva as before. Able to swallow.

Breathing: Really good clearing cough, which was not possible a few minutes before.

After half an hour she was eating with a spoon a large plate of greens, potatoes and meat, and was able to stand by herself (*see figs.*).

Five hours later the effect of the prostigmin had worn off and she was unable to swallow, had almost complete ophthalmoplegia, and was becoming more expressionless.

A further similar injection was given, and in fifteen minutes she was able to finish her supper without trouble.



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The thymus on section was normal, and weighed 5.5 grammes.

Subacute Nephritis.—A. P. NORMAN, M.B., for DONALD PATERSON, F.R.C.P.

C. M., male, aged 5½ years, born 13.11.40.

Previous history and family history not relevant.

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Albumin 260 mg.

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W.B.C. 500,000

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} in 24 hours.

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Blood urea 36 mg./100 c.c.

October 1945: Purpuric spots still present: Melæna. Loud systolic apical murmur, and enlargement of the heart, child extremely ill. Later in the same month developed a right pleural effusion. Then gradual improvement was noticed, fall in temperature, diminution of hæmaturia.

Blood urea 128 mg./100 c.c. Plasma proteins 4.9%.

From January till March 1946 he was in bed at home.

March 1946: General condition good.

Urine: Addis count:

Vol. 340 c.c. in 12 hours.

Albumin 120 mg.

R.B.C. 1,054,000

W.B.C. 102,000

Casts 68,000

} in 24 hours.

B.S.R. 9 mm. in 1 hour.

Urea clearance 100% of normal.

Blood urea 38 mg. %.

Plasma proteins 5.74 grammes %.

Blood-pressure 120/80.

X-ray chest: Heart and lungs normal.

Chronic Nephritis and Renal Dwarfism.—A. P. NORMAN, M.B., for DONALD PATERSON, F.R.C.P.

B. C., male, aged 7½ years, born 26.9.38.

History of polyuria, bed-wetting and excessive thirst for eighteen months. At the onset he had pains in the legs for which he was kept in bed.

Previous history.—Discharging ears at the age of 2 years.

On examination.—Small child, symmetrical build, wizened face, no evidence of rickets. Blood-pressure 130/80.

Urine: Addis count:

Vol. 525 c.c. in 12 hours.
S.G. 1005
Albumin 10 mg.
R.B.C. absent
W.B.C. 105,000
Casts absent

} in 24 hours.

B.S.R. 51 mm. in first hour.

Urea clearance 38% of normal.

Serum calcium 10.5 mg./100 c.c.

Plasma chlorides 675 mg. %.

Plasma bicarbonate 34.7 vols. CO₂.

Blood urea 101 mg. %.

Nephrosis.—A. P. NORMAN, M.B., for DONALD PATERSON, F.R.C.P.

D. R., male, aged 4 years.

History.—Since May 1945 recurrent puffiness of face. He never had obvious hæmaturia, nor constitutional disturbance.

July 1945: Admitted to Chatham Hospital, where blood-pressure was 105/65. Blood urea 31 mg. %. Urine: Albumin, casts and R.B.C.s present.

December 1945: Mild degree of generalized œdema. Bilateral aural discharge.

January 1945: Admitted Great Ormond Street. B.S.R. 51 mm. in first hour. Blood urea, 21 mg./100 c.c. Throat swab, *Strep. viridans*. Blood cholesterol, 368 mg./100 c.c. plasma.

Urine: Addis count:

Vol. 180 c.c. in 12 hours.
Albumin 800 mg.
R.B.C. 1,980,000
Casts 72,000

} in 24 hours.

Plasma proteins:

Albumin per cent. 1.52

Globulin per cent. 1.85

Fibrinogen per cent. 0.48

Total per cent. 3.85

26.1.46: Tonsillectomy, preceded and followed by course of penicillin, ten days in all. 7,000 units four-hourly.

March 1946: Face puffy, otherwise condition good, lively.

Urine: Addis count:

S.G. 1023
Albumin 1,800 mg. %
R.B.C. 284,000
W.B.C. 35,200
Casts 28,400

} in 24 hours.

Blood-pressure 120/80.

B.S.R. 45 mm. in first hour.

Urea clearance 240% of normal.

Bronchiectasis Involving all Lobes of Both Lungs Treated by Lobectomy and Multiple Segmental Resections.—Professor R. S. PILCHER, F.R.C.S.

M. O. F., female, born 5.11.32.

History of persistent cough and winter exacerbations since the age of 4 when she had measles and whooping-cough. She had also had a deformity of the front of the chest since this illness. At 10 years of age she was thought to be suffering from bronchiectasis and was admitted for investigation.

Bronchograms showed extensive bronchiectasis affecting on the right side the middle lobe, pectoral segment of the upper and basal segments of the lower, on the left side the lingula and basal segments of the lower lobe. In spite of all lobes being affected there were many segments free of disease and it was decided to attempt radical treatment by multiple segmental resections.

The child was prepared for operation by postural drainage and breathing exercises. She also had her tonsils and adenoids removed and had a bilateral Caldwell-Luc operation. The first operation on the chest was not undertaken until more than a year after diagnosis.

9.11.44: *First operation.*—Right middle lobectomy and resection of the pectoral segment of the upper lobe. It was decided to defer the lower lobe resection. Recovery was straightforward with rapid re-expansion of the residue of the lung.

23.11.44: *Second operation.*—Segmental resection of the right lower lobe with conservation of dorsal segment. There was some delay in re-expansion of the dorsal segment of

the lower lobe but recovery was otherwise straightforward and postoperative bronchogram showed all residual segments re-expanded and no bronchiectasis on the operated side.

The child was allowed to go home for a few months and continued her breathing exercises and postural drainage.

3.1.46: *Third operation*.—Resection of lingula and basal segments of left lower lobe with conservation of dorsal segment. Again there was some delay in re-expansion of the dorsal segment but recovery was otherwise straightforward. Postoperative bronchogram showed residue of both lobes re-expanded and no bronchiectasis.

Vital capacity.—21.10.44: 1,680 c.c. after pre-operative preparation.

25.2.46: 1,220 c.c. after completion of treatment.

Multiple Cysts of the Right Lung and the Right Bronchus.—Professor R. S. PILCHER, F.R.C.S.

R. S., male, born 5.7.39.

In June 1943 he had what was thought to be a right-sided pneumonia and after this had a series of febrile illnesses until January 1945 when he was first seen at Great Ormond Street Hospital. At that time X-ray showed several cysts with fluid levels in the right lung. Since the first illness X-rays had been taken on several occasions and these showed cysts in the right lung varying in size and in their fluid content. The child was kept under observation for several months during which further variations in the X-ray appearances were seen. Bronchograms showed no abnormality except apparent displacement of the bronchi of the right lung by the cysts.

It was thought that there were multiple cysts or a single loculated cyst in the right lung subject to two complications, inflation and infection. As the child had already had several illnesses attributable to these complications it was decided to attempt resection of the diseased part of the lung.

20.9.45: *First operation, resection of cysts*.—Only one large loculated cyst was clearly identified and this was resected with an area of surrounding lung, the main bronchial communication being sutured.

The child made a straightforward recovery but about a month after operation routine X-ray showed what was thought to be a large pneumothorax on the right side, the possibility of a large distended cyst being also considered. There were no symptoms associated with this finding. A large volume of air was aspirated from the right side of the chest and subsequent X-ray showed re-expansion of the lung. Some days later when he was apparently quite well he suddenly cried out and was found very dyspnoeic and fighting to get his breath. Respiration was loud with inspiratory stridor, and cough which had previously been normal was high pitched. There was displacement of the trachea to the left but breath sounds were equal on the two sides and accompanied by loud rhonchi. The dyspnoea subsided spontaneously in a short time but the change in the quality of the cough persisted. It was remarked that the only occasion on which such a cough had been heard before was in a child with compression of the trachea by a bronchial cyst.

In view of these two episodes it seemed probable that there were more cysts in the lung and it was decided to perform a pneumonectomy.

22.11.45: *Second operation, right pneumonectomy*.—One large cyst was seen on the front of the upper lobe. On exposure of the hilum of the lung a tense cyst was found compressing the main bronchus and apparently growing from its wall. It was possible to clear and divide the bronchus above the cyst.

Recovery from operation was straightforward.

Examination of the specimen showed that the cyst was growing from the upper surface of the eparterial bronchus. It is not obvious why the attack of dyspnoea was so sudden. The cyst contained fluid and had not apparently been distended with air.

Vital capacity.—20.7.45: 1,040 c.c. before operation.

11.1.46: 850 c.c. after pneumonectomy.

Calcium Infarction of Renal Tubules in Infancy.—Pathological Specimens shown by REGINALD LIGHTWOOD, M.D.

Clinical history.—V. C., born June 1945, second child of normal parents, was reared on a patent dried-milk food until 6 months old, when gruel and tinned vegetables were given. Shortly afterwards she began to vomit and the mother suspected the vegetables. After a couple of weeks the vomiting diminished without ceasing. At 7 months brought for

Chronic Nephritis and Renal Dwarfism.—A. P. NORMAN, M.B., for DONALD PATERSON, F.R.C.P.

B. C., male, aged 7½ years, born 26.9.38.

History of polyuria, bed-wetting and excessive thirst for eighteen months. At the onset he had pains in the legs for which he was kept in bed.

Previous history.—Discharging ears at the age of 2 years.

On examination.—Small child, symmetrical build, wizened face, no evidence of rickets. Blood-pressure 130/80.

Urine: Addis count:
 Vol. 525 c.c. in 12 hours.
 S.G. 1005
 Albumin 10 mg.
 R.B.C. absent
 W.B.C. 105,000
 Casts absent

B.S.R. 51 mm. in first hour.
 Urea clearance 38% of normal.
 Serum calcium 10.5 mg./100 c.c.
 Plasma chlorides 675 mg.%.
 Plasma bicarbonate 34.7 vols. CO₂.
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[April 4, 1946]

MEETING HELD AT THE NATIONAL HOSPITAL, LONDON

Epileptiform Attacks of Sensations of Taste and Smell: Unilateral Parkinsonian Tremor (Undiagnosed).—G. I. C. INGRAM, M.B., M.R.C.P., for J. PURDON MARTIN, M.D., F.R.C.P.

D. S., aged 30. Four years: attacks of sensation of taste and smell, associated with an alteration of his perception of his environment and with an interference with his train of thought, and with a feeling of fear and with generalized "gooseflesh".

Two years: Parkinsonian type tremor beginning in left arm spreading to left leg three months ago.

Known to have had papillœdema since 1944.

On examination.—Chronic papillœdema, left more marked than right. Left homonymous field defect.

Defective movement of upper and lower left face with set facies. Parkinsonian tremor left arm and leg and set facies.

Investigations.—E.E.G. suggests deep lesion right hemisphere.

Operation by Mr. Harvey Jackson.—Extensive removal of large temporal astrocytoma which extended into the roof of the temporal horn and the floor of the right lateral horn and adjoining structures; subtemporal decompression.

From then on the Parkinsonian tremor in the patient's left arm subsided and the patient improved considerably. Inco-ordination in both left limbs, but there is only slight loss of perception and motor power.

Thoraco-axillary Inlet Syndrome.—G. I. C. INGRAM, M.B., M.R.C.P., for J. PURDON MARTIN, M.D., F.R.C.P.

Mrs. P. R., aged 33. Two and a half and three and a half years ago had her babies: the younger, a boy, was heavy as an infant. She carried them on her left arm.

November 1944 noticed loss of ability to make accurate small movements with the fingers of the left hand.

January 1945 began to notice wasting in the left hand, starting in the thenar eminence and gradually spreading across the palm.

No sensory or trophic symptoms. No pain at all.

Although she has used the other arm for heavy work since the summer, the wasting has progressed in the last six months.

Some attacks of numbness in the right hand at night since January 1946.

On examination.—Severe wasting of T 1 muscles of left hand. No sensory or trophic changes. No changes in the right hand, but easy occlusability of radial pulses on raising either wrist above the shoulder. Left clavicle flatter than the right.

Operation by Mr. Harvey Jackson.—The scalenus anticus fascia was in such a position as to obstruct and press the subclavian artery in an upward direction; and the brachial plexus was compressed between the clavicle and the first rib. The artery was freed by division of the scalenus anticus and the first rib was divided. The patient made an uneventful recovery as far as the operation was concerned but, at the time of discharge,

consultation, because she was losing weight and still liable to vomit, also pale, constipated, and taking feeds very slowly. Vitamins: Given halibut oil, 3 drops a day from 6 weeks old to 5 months old.

18.1.46: *Outpatient*.—Examination: Aged 7 months, weight 14½ lb. General condition poor. Looked ill. Wasted, fretful. Muscles flabby. Divarication of recti. Slight dehydration. No other physical signs. Urine (fresh, non-catheter specimen): Pale yellow: Sp. gr. 1006. Neutral. Trace of albumin. No sugar. Small flocculent deposit, which on microscopical examination showed no casts or red corpuscles, but numerous pus cells and some epithelial cells, a few uric acid crystals, bacilli and cocci. Blood: R.B.C. 4,110,000; Hb. 64%, C.I. 0.79; W.B.C. 9,600; Polys. 36%, basos. 0.5%, lymphos. 56%, large monos. 7.5%.

The infant was admitted to hospital on 1.2.46, aged 7½ months, with a provisional diagnosis of *calcium infarction of renal tubules*: Pale, wasted, lethargic, a weak cry, constipated, slightly inelastic skin. She took her feeds erratically, vomited occasionally and failed to gain. Five days later she developed an infection, the cause of which was not discovered; with sulphamezathine the temperature fell, but still she did not gain.

From 7.2.46 ultraviolet light was given, without benefit. On 13.2.46 the temperature rose again. Sulphamezathine given for four days, and penicillin for eighteen days. She went downhill, and by 16.2.46 looked very ill. The stools became relaxed and soon the constipation had been replaced by diarrhoea. As no source of infection had been discovered, the mastoids were explored under a local anaesthetic, with negative results, on 20.2.46. She died one month after admission in spite of intravenous therapy, blood transfusions, &c.

Pathological findings in hospital.—Urine: 21.1.46. Sp. gr. 1006. Alb. trace; reaction neutral. No casts or R.B.C. Pus cells +++. Epithelial cells +. A few uric acid crystals. *B. coli* and streps.

1.2.46: Neutral. Alb. 10 mg.%. No deposit.

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12.2.46: Acid. Alb. 10 mg.%. Pus cells 2 per high power field.

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Chest X-ray.—22.2.46: Negative. Mantoux 1/1,000 negative.

In brief, the clinical picture was that of marasmus, with occasional vomiting, constipation, poor appetite, hypotonia, lethargy, and a tendency to dehydration out of proportion to the vomiting. The results of investigation did not seem to account for her condition. The urine was sometimes reported as "normal", and at other times contained traces of albumen, occasional pus cells but no infection; epithelial cells reported in one specimen. The blood urea was somewhat above the upper limit of normality. She died of an intercurrent infection.

Autopsy (Dr. MARTIN BODIAN).—No focus of infection was found. There was oedema of the brain and lungs. The liver showed gross fatty change with faint nutmeg pattern. The kidneys weighed 38 grammes each. Capsules stripped easily. Cortex pale yellow. Pyramids congested. Some degree of foetal lobulation. On cutting into the kidneys there was a gritty feel; the surface of the cross section showed numerous fine greyish-yellow specks in the pyramids especially towards the boundary zone. X-ray of the specimen showed that this material was radio-opaque.

Histology.—Capsule: Normal. Cortex: Many foetal glomeruli. Marked cloudy swelling of convoluted tubules with hyaline casts in many of them. Occasional glomeruli and convoluted tubules showed deposition of calcium sand. *Medulla-pyramids*: Cloudy swelling of collecting tubules with fair number of casts. Also some collecting tubules dilated with desquamation of epithelium and deposition of calcium in lumina. This was the principal distribution of the calcium but some deposits lay outside the tubules. There was no foreign body reaction around these deposits and no evidence of fibrosis. Von Kossa's stain confirmed that the deposits consisted of calcium salts.

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Tuberculous Spine with Paraplegia.—V. C. SNELL, F.R.C.S.

D. W., female, aged 21, October 1941 complained of aching in back. Treated at Ealing Hospital with infra-red rays and massage.

X-ray (18.2.42) showed partial collapse of D.V.7, which was followed one week later by developing paraplegia. Past history of weakness of left leg. ? Anterior poliomyelitis in early childhood. Patient admitted to St. Vincent's 23.2.42. 27.2.42: Seen by Dr. Purdon Martin. Right plantar reflex extensor. Left not obtainable. Loss of sensation right side D.7 to L.1, left side D.7 to L.4. Postural sense and pyramidal tracts unaffected. 11.3.42: Put on spinal frame. 1.5.42, Dr. Purdon Martin: Sharp sensory level at junction of D.5 and D.6 distribution. Severe loss of sense of position of both feet. Suggest spinal laminectomy to relieve pressure on cord. 23.7.42: Operation by Mr. Snell. D.6 and D.7 drilled to relieve pressure. No pus found.

On 27.7.42 still no improvement in deep reflexes, but some improvement in sensation. 20.11.42, Dr. Purdon Martin: No spinal function. Complete loss of all sensation below level of D.6. Still gross loss of joint sense on either side. Suggest decompression operation.

31.12.42: Operation by Mr. Holmes Sellors. Right costo-transversectomy. Rib was removed from its head from about $\frac{3}{4}$ in. and a large abscess cavity was found underneath. Pleura on the outer side was thickened and in some places calcified and at least a gramme of semicaseous pus was mopped from the wound. The long spinal muscles, which had been retracted inwards, were sutured back and the skin closed.

19.2.43, Dr. Purdon Martin: Still no definite sign of recovery in the cord, but spasms less. 21.5.43, Dr. Purdon Martin: There is some pain sensation, and heat and cold sensation in the right foot. 23.8.43: Report on X-ray. The paravertebral abscess is smaller, there is further kyphos with increased destruction of D.5. 15.11.43, Dr. Purdon Martin: No voluntary movements in lower limbs. Small area of superficial sensation at back of right heel. Legs spastic and all reflexes exaggerated. Some slight sense of position in right lower limb. 3.2.44: Movement returning in both legs, right better than left. 13.3.44: Great improvement in lower limbs. There are now signs of recovered function in all tracts of the spinal cord. Can make good flexion movements with both legs, though there is still a good deal of spasticity in the right, and plantar reflex is still extensor. Pain sensation improved. Position at large joints appreciated, but not toes. To have passive movements to both lower limbs daily in addition to massage. 11.5.44: X-ray shows some consolidation in the spinal lesion. 17.7.44: Improvement continues. Can now recognize position of toes. 20.7.44: To be measured for back support. 11.9.44: Right plantar reflex flexor. No spasticity in either leg. 15.10.44: Commenced walking. 16.3.45: Discharged, wearing double iron and toe-lifting strap on left leg.

Disseminated Sclerosis in one of Uniovular Twins, the other Twin being Similarly Affected.—DENIS WILLIAMS, M.D.

D. C., aged 42, married woman with one healthy child aged 12.

Family history.—Nothing of note except for a similar illness in an identical twin. She has 4 other siblings who are well.

History.—Twelve years ago rapid onset of numbness and loss of sensation in left arm and leg; stiffness of muscles and clumsiness of movement. Partial recovery. Two attacks of double vision, eight and six years ago. Four years ago intermittent pain typical of trigeminal neuralgia; progressive ataxia. Paraplegic symptoms have progressed until the present.

Present condition.—Trigeminal neuralgia in second division on left side (intermittent for the last four months). Clumsiness of left hand and, to a less extent, of right; difficulty in walking and stiffness of legs. Occasional urgency of micturition and constipation.

Past history.—Total hysterectomy three and a half years ago.

On examination.—Cranial nerves and optic discs normal. No nystagmus. Upper limbs—wasting of left arm. Inco-ordination left > right with intention tremor on both sides. Tone increase on left; all tendon-jerks, brisk left > right. Sensation—slight impairment to joint sense, light touch and 2-point discrimination on left. Lower limbs—severe spastic paraplegia; increased jerks, ankle clonus, left > right, and bilateral extensor plantar responses; relative sparing of all forms of sensation. Appreciation of joint sense and light touch slightly impaired in left leg.

W.R. negative. Blood-count normal.

it was too early to see how far her neurological condition had been affected. Power of the intrinsic muscles of the left arm had been very slightly improved.

Lateral Column Degeneration following Nutritional Defects While Prisoners of War in the Far East. Two Cases.—G. I. C. INGRAM, M.B., M.R.C.P., for GEORGE RIDDOCH, M.D., F.R.C.P.

F. A., aged 33; A. W., aged 27. These patients were fed on a diet chiefly of polished rice, and developed symptoms of mental disturbance, visual errors, muscular weakness, bladder incontinence, skin lesions, glossitis and mouth sores, and now show a pure pyramidal lesion affecting the lower legs.

Functional Recovery following Common Peroneal Nerve Suture. Three Cases.—J. E. A. O'CONNELL, F.R.C.S.

(1) H. B., male, aged 49, sustained extensive lacerations of the right calf and popliteal region with an immediate complete lesion of the right common peroneal nerve. At operation (18.5.42) eleven months after injury, a complete lesion with a gap was found and secondary suture performed. Motor recovery commenced four months after operation and progressed satisfactorily.

(2) J. G., male, aged 32, sustained multiple injuries in an air raid, including a laceration in the left popliteal space with an immediate complete lesion of the left common peroneal nerve. At operation (21.3.41) six months after injury, a lesion in continuity with no sparing of fibres was found, excised and secondary suture performed. Motor recovery commenced eleven months after operation and progressed satisfactorily.

(3) G. E., male, aged 32, sustained G.S.W. lateral aspect of right leg with an immediate complete lesion of the right common peroneal nerve. At operation (26.5.45) three and a half months after injury, a lesion in continuity containing several shell fragments was found, excised and secondary suture performed. Motor recovery commenced four months after operation and is progressing.

Comment.—These cases have been shown in order to demonstrate the inaccuracy of the opinion that functional recovery after common peroneal nerve suture is extremely unusual and of poor quality should it occur. They indicate the need for a more rational approach to prognosis as regards motor recovery after peripheral nerve suture. It is not, as might be imagined from what is frequently written on the subject, that some nerves possess an inherent quality which leads to good motor recovery after suture. Rather is it that the extent of motor recovery which follows nerve suture carried out in favourable circumstances is directly proportionate to the size of the muscles which it supplies and the amplitude of the movements which they produce. Thus motor recovery in the muscles of the thigh and upper arm has been excellent after suture of the femoral and musculocutaneous nerves—in one case good function following an inlay cable graft of the latter nerve. In the muscles of the lower leg and forearm useful recovery can be expected. But in the case of the small muscles of the foot and hand the outlook is very different. Recovery of function in the intrinsic muscles of the foot after sciatic nerve suture is probably unknown and, except in lesions of the median and ulnar nerves close to the wrist, useful recovery of function in the small muscles of the hand must be a most unusual occurrence.

Recovery following Suture of Peroneal Nerve.—V. C. SNELL, F.R.C.S.

J. C., female, aged 33. Attended hospital in 1941, with a history of having fallen through a shop window eighteen years previously, sustaining extensive lacerations to the left leg. The foot was fixed in plantar flexion, and the patient complained of aching in the foot and that she caught her foot in carpets, &c.

On 26.2.42 Dr. Purdon Martin recommended exploration of the common peroneal nerve, if the galvanic response was satisfactory. If there was no response, fixation of the foot was planned. There was no response from the tibialis anticus.

25.6.42: *Operation.*—The lower scar was explored. The peroneal nerve was found to be involved in scar tissue and it was divided. Both ends were involved in scar tissue. The ends of the nerve were resected, and the nerve resutured. The knee was plastered at a right angle.

26.8.43: *Operation.*—Right tibialis anticus lengthened by slide operation. Limb plastered.

All muscles are now working. She can walk quite comfortably without any splint or toe-raising spring. She has no pain or aching in the leg.

Tuberculous Spine with Paraplegia.—V. C. SNELL, F.R.C.S.

D. W., female, aged 21, October 1941 complained of aching in back. Treated at Ealing Hospital with infra-red rays and massage.

X-ray (18.2.42) showed partial collapse of D.V.7, which was followed one week later by developing paraplegia. Past history of weakness of left leg, ? Anterior poliomyelitis in early childhood. Patient admitted to St. Vincent's 23.2.42. 27.2.42: Seen by Dr. Purdon Martin. Right plantar reflex extensor. Left not obtainable. Loss of sensation right side D.7 to L.1, left side D.7 to L.4. Postural sense and pyramidal tracts unaffected. 11.3.42: Put on spinal frame. 1.5.42, Dr. Purdon Martin: Sharp sensory level at junction of D.5 and D.6 distribution. Severe loss of sense of position of both feet. Suggest spinal laminectomy to relieve pressure on cord. 23.7.42: Operation by Mr. Snell. D.6 and D.7 drilled to relieve pressure. No pus found.

On 27.7.42 still no improvement in deep reflexes, but some improvement in sensation. 20.11.42, Dr. Purdon Martin: No spinal function. Complete loss of all sensation below level of D.6. Still gross loss of joint sense on either side. Suggest decompression operation.

31.12.42: Operation by Mr. Holmes Sellors. Right costo-transversectomy. Rib was removed from its head from about $\frac{3}{4}$ in. and a large abscess cavity was found underneath. Pleura on the outer side was thickened and in some places calcified and at least a gramme of semicaseous pus was mopped from the wound. The long spinal muscles, which had been retracted inwards, were sutured back and the skin closed.

19.2.43, Dr. Purdon Martin: Still no definite sign of recovery in the cord, but spasms less. 21.5.43, Dr. Purdon Martin: There is some pain sensation, and heat and cold sensation in the right foot. 23.8.43: Report on X-ray. The paravertebral abscess is smaller, there is further kyphos with increased destruction of D.5. 15.11.43, Dr. Purdon Martin: No voluntary movements in lower limbs. Small area of superficial sensation at back of right heel. Legs spastic and all reflexes exaggerated. Some slight sense of position in right lower limb. 3.2.44: Movement returning in both legs, right better than left. 13.3.44: Great improvement in lower limbs. There are now signs of recovered function in all tracts of the spinal cord. Can make good flexion movements with both legs, though there is still a good deal of spasticity in the right, and plantar reflex is still extensor. Pain sensation improved. Position at large joints appreciated, but not toes. To have passive movements to both lower limbs daily in addition to massage. 11.5.44: X-ray shows some consolidation in the spinal lesion. 17.7.44: Improvement continues. Can now recognize position of toes. 20.7.44: To be measured for back support. 11.9.44: Right plantar reflex flexor. No spasticity in either leg. 15.10.44: Commenced walking. 16.3.45: Discharged, wearing double iron and toe-lifting strap on left leg.

Disseminated Sclerosis in one of Uniovular Twins, the other Twin being Similarly Affected.—DENIS WILLIAMS, M.D.

D. C., aged 42, married woman with one healthy child aged 12.

Family history.—Nothing of note except for a similar illness in an identical twin. She has 4 other siblings who are well.

History.—Twelve years ago rapid onset of numbness and loss of sensation in left arm and leg; stiffness of muscles and clumsiness of movement. Partial recovery. Two attacks of double vision, eight and six years ago. Four years ago intermittent pain typical of trigeminal neuralgia; progressive ataxia. Paraplegic symptoms have progressed until the present.

Present condition.—Trigeminal neuralgia in second division on left side (intermittent for the last four months). Clumsiness of left hand and, to a less extent, of right; difficulty in walking and stiffness of legs. Occasional urgency of micturition and constipation.

Past history.—Total hysterectomy three and a half years ago.

On examination.—Cranial nerves and optic discs normal. No nystagmus. Upper limbs—wasting of left arm. Inco-ordination left > right with intention tremor on both sides. Tone increase on left; all tendon-jerks, brisk left > right. Sensation—slight impairment to joint sense, light touch and 2-point discrimination on left. Lower limbs—severe spastic paraplegia; increased jerks, ankle clonus, left > right, and bilateral extensor plantar responses; relative sparing of all forms of sensation. Appreciation of joint sense and light touch slightly impaired in left leg.

W.R. negative. Blood-count normal.

[May 2, 1946]

MEETING HELD AT THE NATIONAL HOSPITAL, QUEEN SQUARE, LONDON
 SYMPOSIUM ON THE SURGICAL TREATMENT OF MYASTHENIA
 GRAVIS

Mr. Geoffrey Keynes said that he believed the main purpose of this meeting was to provide a clinical demonstration of the results of thymectomy for myasthenia gravis, over 30 patients having been assembled for inspection by the members of the Section. He would therefore confine his remarks to an attempt to assess the results and to draw attention to some of the factors which seemed to influence them.

The first question that any physician would naturally ask was what was the mortality of the operation. Mr. Keynes said he had now performed the operation 63 times, but that it was not possible to express the mortality as a percentage of this figure. If the figures were scrutinized chronologically it would be seen that there had been 7 post-operative deaths among the first 21 patients, but only 2 among the next 42. That is to say, it appeared that with increased experience of the operation and post-operative management, the danger had been reduced to a very low figure. This was partly to be attributed to the advice given by Blalock in his original paper to supply the patient after operation with plenty of fluid by means of an intravenous drip. This may have been necessary in the hot climate of Baltimore, but in London it seemed to promote the excessive secretion of mucus to which myasthenic patients were liable, and so to increase the danger to life. This measure had now for some time been omitted.

In addition to the 9 post-operative deaths 4 others had died of the disease, giving a total of 13 patients dead. In 9 others the operation was still too recent for assessment of the result. This left 41 to be assessed. The present figures submitted by Dr. Carson were as follows:

A. Apparently cured, not taking prostigmin	14
B. Very much better, taking small dose of prostigmin	15
C. Slight improvement	3
D. No improvement	9
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These results had now been established for periods up to four years, and Mr. Keynes challenged anyone to produce equal results by means of medical treatment or spontaneous remission in any comparable series of patients. All the patients hitherto submitted to operation had been described as severe or very severe examples of the disease. The milder ones had not so far been accepted for surgical treatment.

The results were admittedly erratic, and the reasons for this were still obscure. But scrutiny of the series showed that, on the whole, the best results were obtained in the younger patients with short histories, and the poor results in the older patients with long histories. It was also noticeable that some symptoms, particularly ptosis, tended to remain, even when the patient as a whole had greatly improved.

One factor that plainly influenced the results adversely was the incidence of thymic tumours. There had been 7 of these among the 63 patients, and they inevitably made the operation more difficult and dangerous, owing to their being closely adherent to the pleura and neighbouring structures. Sometimes removal of a thymoma produced great improvement at first, but this might be followed soon by complete relapse and death.

Apart from the presence of a tumour, the size of the gland had no relation to the severity of the disease. The weight varied from 3 to 30 grammes. The histological findings were becoming more definite, and Dr. Collins would describe these.

Mr. Keynes had often been told in past years that myasthenia gravis did not occur in children. Nevertheless the age of his patients had ranged from 56 to 2 years. Recently two patients aged 4 and 2, had been operated on at Great Ormond Street Hospital, under the care of Dr. Wyllie. Both children were moribund when admitted, but had responded to prostigmin, and since operation had recovered completely except for persistent ptosis in one of them. The child of 4 was now described by her father as "tireless".

As a pendant to his remarks Mr. Keynes referred to a communication he had received from Dr. Viets, of the Massachusetts General Hospital, Boston. Dr. Viets had submitted 16 patients to operation but for the time being had abandoned this form of treatment. Mr. Keynes suggested that this was probably due to two factors: (1) the operative mortality of 5 in 16, the same rate as in the first 21 of Mr. Keynes' patients, (2) the high incidence of tumours, also 5 in 16, a factor which Mr. Keynes had already shown to influence results adversely.

The taking of prostigmin after operation was influenced to some extent by the psychology of the patients. On the one hand there were some who were so determined to register improvement that they tended to reject prostigmin even when they really needed it. On the other hand there were those who had become so habituated to the drug that they had a feeling of insecurity without it, even when it was not necessary. The second category was illustrated by one of the patients present at the demonstration, who was taking "one tablet a week", this being on Saturday afternoons with a view to a dance in the evening.

Mr. Keynes concluded that the results he had obtained on the whole justified the further performance of thymectomy. There was also evidence in favour of operating early, now that the operation had become almost safe, before the disease had become chronic. Early operation might also forestall the formation of thymomas, the high incidence of which was a serious factor influencing results.

Dr. Douglas H. Collins: *Notes on the pathology of the thymus glands removed in the surgical treatment of myasthenia gravis.*—Perhaps the scarcity of morbid appearances is the most astonishing feature in the pathological anatomy of the thymus glands removed from patients with myasthenia gravis. Gross structural abnormalities of the gland are the exception rather than the rule. Tumours of the gland, as will be shown, occur only in a proportion of 1 in 7 of the cases. The remaining glands differ hardly at all from the normal in their appearance to the naked eye, though there are some qualitative differences in their histology.

Dr. A. B. Bratton and I are examining these glands together. Our series and its statistical analysis are not yet complete; a more detailed paper will be published elsewhere. There are certain features of the glands constant enough to enable us to state with some confidence whether or not a gland comes from a case of myasthenia gravis when examining unlabelled sections under the microscope. It may be of value at this stage to describe in broad terms some of the pathological characteristics of the thymus in myasthenia gravis, so that they may be here recorded.

There are three main headings: (1) The normal thymus; (2) thymic tumours in myasthenia gravis; (3) non-tumour glands from myasthenic cases. In all we have so far examined 56 glands from patients with myasthenia, two of which came to post-mortem before operation, and a number of normal glands as control material.

The normal thymus.—Normal thymus glands for control purposes have been sought amongst Dr. Bratton's large material and also in my own small series of 10 healthy persons who died sudden, accidental deaths. Ordinary hospital post-mortem material does not provide satisfactory controls as atrophy of the thymus occurs very rapidly in malnutrition, infective, or cachectic diseases. Amongst normals the weight of the individual thymus is extremely variable. The shape is somewhat more constant according to age-group, varying from a solid conoid or cordate gland in infancy to the elongated bilobed gland of the adult. Qualitative changes, best seen under the microscope, also tend to be constant in the different age-groups. At adolescence fat replacement along the lines of the fibrous intersections of the gland commences and advances into the typical adult type in which only islets of thymic tissue are found floating in fat. These islets in the normal person are mainly of medullary tissue. Hassall bodies persist and probably continue to be formed throughout adult life, though cornification and calcification of these may be seen at any age. The large lymphoid cortical foci seen in the childhood gland are reduced in adult life to only a thin rim of lymphocytes or an occasional small rounded follicle. The small lymphocytes, or thymocytes, become less closely packed in the adult medullary tissue. It is particularly noteworthy that the amount of parenchymatous tissue in a gland cannot be assessed without microscopic section, and that a gland which to the naked eye looks solid and fleshy may, on section, be found to have only some 20 to 40% of glandular tissue. Bratton has used a method of floating a gland in water as a rough assessment of this, the infiltrated fat lending buoyancy to the organ.

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Thymic tumours in myasthenia gravis.—Tumours of the gland recognizable either by the naked eye or by the microscope have been found in only eight cases (14.3%). They have been found more commonly in the severer forms of the disease. These tumours have not been uniform in type. They are sometimes localized in one part of the organ or diffused through the whole. Their histology varies within the range of cell types described as lympho-epithelioma or thymoma.

From a survey of the literature it would appear that the incidence of myasthenia gravis in cases of thymic tumour is much greater than the incidence of thymic tumours in cases of myasthenia.

Non-tumour, thymus glands in myasthenia gravis.—In myasthenia gravis, apart from glands containing tumour, the thymus does not differ in size or in gross appearance from the normal adult type and it does not markedly differ in the percentage of parenchymatous tissue in relation to fat and stroma substance. The conception of persistent thymus should, therefore, I think, be abandoned, but microscopically there are two characteristics which differentiate the myasthenic gland from the normal. The first is a qualitative difference in the surviving islets of parenchyma. Most myasthenic glands show a denser concentration of lymphocytes in the cortex, in other words, cortical atrophy is less marked than in the normal. Many islets show well-rounded lymphoid cortical foci and lymphocytes—or as some would prefer to call them, small thymocytes—are more thickly scattered about the medulla. The second characteristic is more peculiar. This is the formation within the medulla of structures apparently identical with the germ centres or secondary nodules of Flemming commonly seen in lymph glands. These are regularly rounded or slightly oval areas of clearer tissue circumscribed by concentric rings of small darkly-staining cells of lymphoid type. In the clear centre there are oval, vesicular, pale, nuclei fairly evenly distributed and lying within large cells whose cell walls and divisions are difficult to demonstrate. The uniformity of this cell mass is interrupted by spaces which may possibly be rudimentary lymphatic channels, but are more likely to be vacuolated degenerating cells containing nuclear fragments. Nuclear mitoses are also often seen in these germ centres, which have been found in two-thirds of myasthenic thymuses (28 out of 42 non-tumour glands) and have been found once in the surviving tissue around a tumour. In silver-stained preparations, these germ centres are not penetrated by the argentophil fibrils which are interlaced among the epithelial tissue of the thymic medulla. Their relation with lymphoid tissue is supported by this fact and by their corona of lymphocytes which are not otherwise so arranged in the medulla. In my opinion the presence of these structures in so many myasthenic glands is statistically significant. They were first described only in 1924 by Jolly and de Tannenberg in the thymus of a normal cat as something quite exceptional. Bratton has seen them in only three instances among a large number of non-myasthenic glands and I have not encountered them among my own normal material.

Hassall bodies do not appear to vary between normal and myasthenic glands. In a few cases of myasthenia gravis one finds also a packed syncytial concentration of clear cells of the medulla which might be regarded either as medullary hyperplasia or as the early formation of germ centres before they collect their lymphocytes.

Interpretation of these findings is impossible at present, but it would seem that the thymus in myasthenia reacts in a manner more characteristic of lymphoid tissue than of an epithelial organ. One cannot postulate a specific function for these germ centres, as we do not know their function in lymph nodes, and in the thymus these structures do not appear different from the secondary nodules or germ centres which appear in many other organs as well as lymph glands; for example, the toxic thyroid, where there is an associated lymphoid infiltration.

SUMMARY

(1) Only a proportion of about 1 in 7 thymus glands bear recognized tumours in a series of cases of myasthenia gravis.

(2) Persistence of the thymus beyond the age of expected involution is a hazy conception and is not one on which the relation between the gland and myasthenia gravis can be explained.

(3) The majority of the glands in myasthenia gravis do not show any gross anatomical abnormality.

(4) Qualitative changes in the histology of non-tumour glands in myasthenia gravis are significantly common. They are such as to indicate a reaction of the pattern charac-

teristic of a lymphoid tissue, but whether these are related to the cause or to the effects of myasthenia gravis cannot be judged.

(5) The tissue elements more specific to the thymus, i.e. reticulated medullary epithelium and the Hassall bodies, have not so far been shown to undergo any constant or significant change in myasthenia gravis except in the case of tumours where both lymphoid and epithelial elements are concerned in the new growth.

Dr. Purdon Martin (Chairman): My first impression was one of disappointment that so many patients were still taking prostigmin. Moreover, we are told that 9 patients who were operated on have not improved, and 3 others only slightly, while 5 died in addition to those who had tumours. From these results it is evident that thymectomy is not the whole answer to myasthenia.

On the other hand, 14 patients are able to do without prostigmin, and lead normal lives, and the results are best in the young people.

We must ask ourselves in the first place what would have been the mortality in these cases if no operations had been performed. The disease is one with which we were quite familiar before the operation was introduced and we can recall what the results were. It was always a more severe disease in the young people. Over a considerable number of years before the introduction of prostigmin I never saw a patient under the age of 25 survive for more than twelve months, and it was rare for them to do anything other than go steadily downhill. It is precisely with these young patients that Mr. Keynes reports his best results. Whether the thymus has anything directly to do with myasthenia or not, for these patients the operation does something which is dramatic and life-saving.

The two children who have been shown are extreme examples of this. It happened that by the kindness of Dr. Wyllie I saw both of them before they were operated on—one of them was just surviving in a Drinker respirator—and making such allowances as my experience permits me to make for the possibility of remission on the point of death, I cannot believe that they would both be as they are this evening, or be here at all, if they had not had the operation. That then is my conclusion as regards the young people.

Of the older patients many, especially since the arrival of prostigmin, passed into a chronic state—sometimes a little better, sometimes a little worse. In many cases only the ocular muscles and face were affected, and in others the muscles of the jaw and throat as well. In such cases the effects of the operation are less definite. We are told that 15 patients improved greatly and 3 others moderately.

A point which should be considered is, when the improvement took place in relation to the operation. If improvement occurred at once, then we should attribute it to the operation, but if it did not occur till some months afterwards, it would be safer in assessing the results to attribute it to the effects of a remission. I feel that Mr. Keynes and Dr. Carson can afford to make that concession to the critics, because recalling my experience of this disease in the past, I can only conclude that on whatever it is based, the operation represents a great advance in the treatment of a disease which had a very high mortality.

Sir Charles Symonds said that, having examined the cases and heard Mr. Geoffrey Keynes's report, he had no doubt that thymectomy represented a very great advance in the treatment of myasthenia gravis. Spontaneous remissions were well known, and he had personal experience of several striking examples, but he was sure that the average expectation of health and life in this disease had been much less than that now offered by surgery. It would, however, be valuable to compare with Mr. Keynes' series, a series of control cases followed over a number of years in the pre-prostigmin days and in the prostigmin period, without operation. Myasthenia gravis was a rare disease, and it would be necessary in any investigation of this sort to pool the experience of neurologists.

Dr. L. P. E. Laurent: Mr. Keynes' patients certainly show some very remarkable examples of complete remission of symptoms, but my experience of myasthenia gravis in the past eighteen years, extending to some 65 cases, has led me to believe that the

Thymic tumours in myasthenia gravis.—Tumours of the gland recognizable either by the naked eye or by the microscope have been found in only eight cases (14.3%). They have been found more commonly in the severer forms of the disease. These tumours have not been uniform in type. They are sometimes localized in one part of the organ or diffused through the whole. Their histology varies within the range of cell types described as lympho-epithelioma or thymoma.

From a survey of the literature it would appear that the incidence of myasthenia gravis in cases of thymic tumour is much greater than the incidence of thymic tumours in cases of myasthenia.

Non-tumour, thymus glands in myasthenia gravis.—In myasthenia gravis, apart from glands containing tumour, the thymus does not differ in size or in gross appearance from the normal adult type and it does not markedly differ in the percentage of parenchymatous tissue in relation to fat and stroma substance. The conception of persistent thymus should, therefore, I think, be abandoned, but microscopically there are two characteristics which differentiate the myasthenic gland from the normal. The first is a qualitative difference in the surviving islets of parenchyma. Most myasthenic glands show a denser concentration of lymphocytes in the cortex, in other words, cortical atrophy is less marked than in the normal. Many islets show well-rounded lymphoid cortical foci and lymphocytes—or as some would prefer to call them, small thymocytes—are more thickly scattered about the medulla. The second characteristic is more peculiar. This is the formation within the medulla of structures apparently identical with the germ centres or secondary nodules of Flemming commonly seen in lymph glands. These are regularly rounded or slightly oval areas of clearer tissue circumscribed by concentric rings of small darkly-staining cells of lymphoid type. In the clear centre there are oval, vesicular, pale, nuclei fairly evenly distributed and lying within large cells whose cell walls and divisions are difficult to demonstrate. The uniformity of this cell mass is interrupted by spaces which may possibly be rudimentary lymphatic channels, but are more likely to be vacuolated degenerating cells containing nuclear fragments. Nuclear mitoses are also often seen in these germ centres, which have been found in two-thirds of myasthenic thymuses (28 out of 42 non-tumour glands) and have been found once in the surviving tissue around a tumour. In silver-stained preparations, these germ centres are not penetrated by the argentophil fibrils which are interlaced among the epithelial tissue of the thymic medulla. Their relation with lymphoid tissue is supported by this fact and by their corona of lymphocytes which are not otherwise so arranged in the medulla. In my opinion the presence of these structures in so many myasthenic glands is statistically significant. They were first described only in 1924 by Jolly and de Tannenberg in the thymus of a normal cat as something quite exceptional. Bratton has seen them in only three instances among a large number of non-myasthenic glands and I have not encountered them among my own normal material.

Hassall bodies do not appear to vary between normal and myasthenic glands. In a few cases of myasthenia gravis one finds also a packed syncytial concentration of clear cells of the medulla which might be regarded either as medullary hyperplasia or as the early formation of germ centres before they collect their lymphocytes.

Interpretation of these findings is impossible at present, but it would seem that the thymus in myasthenia reacts in a manner more characteristic of lymphoid tissue than of an epithelial organ. One cannot postulate a specific function for these germ centres, as we do not know their function in lymph nodes, and in the thymus these structures do not appear different from the secondary nodules or germ centres which appear in many other organs as well as lymph glands; for example, the toxic thyroid, where there is an associated lymphoid infiltration.

SUMMARY

(1) Only a proportion of about 1 in 7 thymus glands bear recognized tumours in a series of cases of myasthenia gravis.

(2) Persistence of the thymus beyond the age of expected involution is a hazy conception and is not one on which the relation between the gland and myasthenia gravis can be explained.

(3) The majority of the glands in myasthenia gravis do not show any gross anatomical abnormality.

(4) Qualitative changes in the histology of non-tumour glands in myasthenia gravis are significantly common. They are such as to indicate a reaction of the pattern charac-

teristic of a lymphoid tissue, but whether these are related to the cause or to the effects of myasthenia gravis cannot be judged.

(5) The tissue elements more specific to the thymus, i.e. reticulated medullary epithelium and the Hassall bodies, have not so far been shown to undergo any constant or significant change in myasthenia gravis except in the case of tumours where both lymphoid and epithelial elements are concerned in the new growth.

Dr. Purdon Martin (Chairman): My first impression was one of disappointment that so many patients were still taking prostigmin. Moreover, we are told that 9 patients who were operated on have not improved, and 3 others only slightly, while 5 died in addition to those who had tumours. From these results it is evident that thymectomy is not the whole answer to myasthenia.

On the other hand, 14 patients are able to do without prostigmin, and lead normal lives, and the results are best in the young people.

We must ask ourselves in the first place what would have been the mortality in these cases if no operations had been performed. The disease is one with which we were quite familiar before the operation was introduced and we can recall what the results were. It was always a more severe disease in the young people. Over a considerable number of years before the introduction of prostigmin I never saw a patient under the age of 25 survive for more than twelve months, and it was rare for them to do anything other than go steadily downhill. It is precisely with these young patients that Mr. Keynes reports his best results. Whether the thymus has anything directly to do with myasthenia or not, for these patients the operation does something which is dramatic and life-saving.

The two children who have been shown are extreme examples of this. It happened that by the kindness of Dr. Wyllie I saw both of them before they were operated on—one of them was just surviving in a Drinker respirator—and making such allowances as my experience permits me to make for the possibility of remission on the point of death, I cannot believe that they would both be as they are this evening, or be here at all, if they had not had the operation. That then is my conclusion as regards the young people.

Of the older patients many, especially since the arrival of prostigmin, passed into a chronic state—sometimes a little better, sometimes a little worse. In many cases only the ocular muscles and face were affected, and in others the muscles of the jaw and throat as well. In such cases the effects of the operation are less definite. We are told that 15 patients improved greatly and 3 others moderately.

A point which should be considered is, when the improvement took place in relation to the operation. If improvement occurred at once, then we should attribute it to the operation, but if it did not occur till some months afterwards, it would be safer in assessing the results to attribute it to the effects of a remission. I feel that Mr. Keynes and Dr. Carson can afford to make that concession to the critics, because recalling my experience of this disease in the past, I can only conclude that on whatever it is based, the operation represents a great advance in the treatment of a disease which had a very high mortality.

Sir Charles Symonds said that, having examined the cases and heard Mr. Geoffrey Keynes's report, he had no doubt that thymectomy represented a very great advance in the treatment of myasthenia gravis. Spontaneous remissions were well known, and he had personal experience of several striking examples, but he was sure that the average expectation of health and life in this disease had been much less than that now offered by surgery. It would, however, be valuable to compare with Mr. Keynes's series, a series of control cases followed over a number of years in the pre-prostigmin days and in the prostigmin period, without operation. Myasthenia gravis was a rare disease, and it would be necessary in any investigation of this sort to pool the experience of neurologists.

Dr. L. P. E. Laurent: Mr. Keynes's patients certainly show some very remarkable examples of complete remission of symptoms, but my experience of myasthenia gravis in the past eighteen years, extending to some 65 cases, has led me to believe that the

prognosis is much better than is generally thought. For instance, of 16 cases who have been followed up by Dr. Mary Walker and myself for more than ten years, 13 are alive to-day. A patient who was in the National Hospital in 1912 with severe symptoms which lasted some seven years, lives to-day at Alton, Hants, where he has worked as a farm labourer for the past thirty years without relapse. Another remarkable patient was a Danish woman who had two acute episodes with respiratory crises lasting several months, and who had shown no trace of myasthenia for eight years when I last saw her.

It seems to me that Dr. Mary Walker's experiment in which she showed that release of a cuff round the arm after exercising the muscles of the forearm was followed by a rapid ptosis, requires some explanation in any theory of the causation of myasthenic symptoms. Any thymic theory must be out of keeping with this experiment.

It is disappointing that the only good prognostic factor after thymectomy should be the short duration of symptoms. The best remission in myasthenia always occurs early, and therefore the early case is always the one most likely to show a good remission even without treatment.

I have recently seen a patient belonging to this present series, a woman of 39 who did not improve after thymectomy. She is certainly suffering from muscular dystrophy, and it would therefore be interesting to know whether her thymus showed any of the slight changes which Dr. Collins has seen in some of the cases of myasthenia.

Dr. P. H. Sandifer: I should like to ask Mr. Keynes how often, in his considerable experience, he has removed thymuses from myasthenics previously treated by radiotherapy; secondly, what was the histological appearance of thymuses previously irradiated; and thirdly, if and when characteristic histological changes were witnessed, whether he noted any relationship between these changes and the dose of X-rays.

My reason for asking this question is that at one time I had under my care a myasthenic patient of Dr. Douglas McAlpine who improved enormously after a course of radiotherapy. Miss Ross gave her, at Mount Vernon Hospital, Northwood, a dose to the thymus of 1,330 r, over nine days. Seven months later thymectomy was performed with still further improvement which has not, however, remained at the previous high level.

At operation an atrophic thymus weighing 8 grammes was removed and the sections from the gland showed only a few patches of active gland tissue, the rest being pink, amorphous material replacing thymic tissue.

I think it is important to know whether it is possible to produce atrophy of the thymus by radiotherapy and, if so, what dose is necessary. Doses much larger than the 1,330 r received by this patient have been given. One patient I referred to Miss Ross received 3,743 r over twenty-one days she does not now need to take prostigmin. Another patient treated by Professor Windeyer at Middlesex Hospital by radiotherapy does not now take prostigmin and another is reducing the dose of prostigmin while at the same time becoming capable of greater exertion. Other patients treated with comparable doses of X-rays, on the other hand, have improved little or not at all.

Section of Radiology

President—W. M. LEVITT, M.D., F.R.C.P.

[March 15, 1946]

The Influence of Wave-lengths on Certain Lesions Produced by the Irradiation of Mice

By A. LACASSAGNE

(Institut du Radium, Paris)

PRELIMINARY CONSIDERATIONS

I SHALL be dealing with the results of various experiments undertaken between 1941 and 1944, some of which, having been temporarily abandoned, have not previously been described. During this period, for obvious reasons, we were obliged to reduce the size of our experimental animals: rabbits, formerly in general use, had to be replaced by mice. This reduction in the size of the subject necessitated a modification of the means employed. In order to adapt the power used to the much lower penetration required when dealing with these very small animals, soft rays—which, indeed, turned out to be suitable for many other reasons—had to be used.

I propose to describe successively lesions caused by (a) K radiation of molybdenum; (b) ultraviolet rays; (c) L radiation of silver.

(a) Irradiation by K Radiation of Molybdenum.

The following experiments, undertaken in collaboration with A. Chamorro, were intended to establish the dose required to induce total sterilization of the ovaries in mice, resulting in complete cessation of cyclic vaginal activity and sexual activity.¹

Female mice two months old were treated with unfiltered rays from a molybdenum anode—effective wave-length 0.95 Å. With a tension of 35 kV., an intensity of 15 mA., and a focal distance of 12 cm., a dose of 3,000 r per minute was measured on the surface of the skin. The mice, anaesthetized with ether, were fixed, ventral surface downwards, on a board. Their bodies were protected by sheets of lead, having perforations in the lumbar region 1 cm. square, each of which corresponded to the site of an ovary.

In this way four groups of mice received respective doses of 3,000, 4,500, 6,000 and 9,000 r in the ovarian region. Two of the 6,000 r group and all the 9,000 r group died less than six weeks later as a result of the experiment. I shall not refer to the purely physiological changes observed in the survivors; I shall briefly indicate the effects of the treatment on the cutaneous tissues, and describe in greater detail the histological changes occurring in some cases in the ovaries and kidneys.

(1) *Cutaneous reactions.*—The only phenomenon which called for notice on examining the skin during the weeks following irradiation was the loss of hair over the area exposed to the rays. This occurred on approximately the same date—about the twentieth day—regardless of the dose. In no case was there any sign of ulceration. There was a sparse growth of new hair in the case of animals receiving doses of 3,000 and 4,500 r, and an extremely feeble scattered growth in those receiving 6,000 r. The depilation remained quite obvious. It was sometimes accompanied, in the case of strong doses, by slight

¹In the series of results published by Parkes, and by Brambell and Parkes (*Proc. Roy. Soc. B*, 1927-28) this "Roentgen castration," achieved long before in the case of rabbits, was not attained.

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FIG. 2.—Left ovary shown in fig. 1 (below). Cross section. $\times 100$.

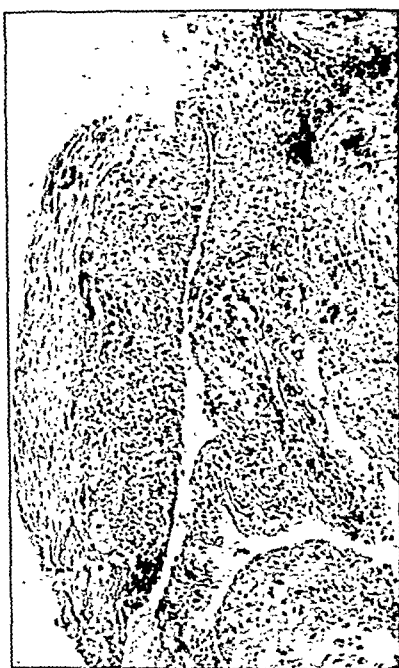
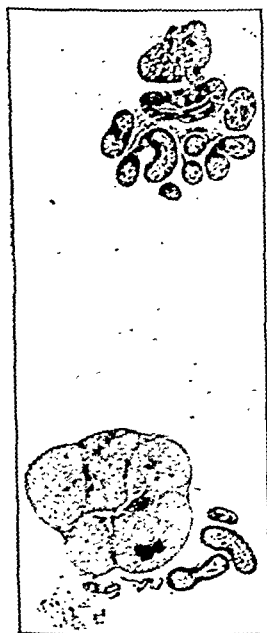


FIG. 3.—Irradiated mouse ovary (K radiation of molybdenum; skin dose 6,000 r) after 583 days. Longitudinal section. $\times 100$.



L.

R.



FIG. 4.—Irradiated mouse kidney (K radiation of molybdenum; skin dose 3,000 r) after 530 days. $\times 100$.

FIG. 1.—Irradiated mouse ovaries (K radiation of molybdenum; skin dose 3,900 r) after 64 days. The left ovary is completely sterilized and atrophied. The right (incorrect irradiation) shows marked hypertrophy, due to the production of structures resembling enormous corpora lutea. $\times 16$.

sclerosis of the cellular-fatty tissue, and even by a slight degree of atrophy of the cutaneous muscle.

(2) *Total sterilization of the ovary.*—The result which we were out to attain was realized in only a small proportion of cases. Eleven mice survived for more than three months. In only three of these cases—two irradiated with 4,500 and one with 6,000 r—was there total atrophy of both ovaries, and consequently of the horns of the uterus and the mammary organs, as well as permanent mucification of the vaginal epithelium. In all, out of a total of sixteen mice—the eleven already referred to and five others which survived long enough to make a histological examination of the ovaries worth while—two only, after a dose of 3,000 r, showed total atrophy, and then of only one gland (fig. 1).

These results seem to show that the chief difficulty in such experiments is to locate the ovaries exactly. In attempting to confine the irradiation to a very restricted field, so as to avoid too heavy a mortality, we rarely succeeded in administering the precise dose required to both ovaries, either because our calculation of the site for irradiation was originally incorrect, or because the subject moved during the course of the experiment. One proof of this is that three mice were subsequently found to be gravid; in two cases, killed before expulsion, the fetuses were found to occupy only one horn of the uterus. Nevertheless, the results so far obtained are sufficient to show that from 3,000 r upwards it is possible to induce total sterilization of the mouse ovary, together with the cessation of all physiological activity—in other words, complete castration.

Histological examination.—The study by successive sections of an ovary sterilized by a dose of 3,000 r, undertaken sixty-four days later, showed considerable atrophy of the organ, which was reduced to a little tongue about a millimetre long by half a millimetre wide, resting on a muscular plane, the medullary surface serving as a hilum, and covered on the other surface and on the edges by the ovarian epithelium, which had not suffered the same retrogression as the rest of the organ, its cells being more closely knit and higher, and definitely prismatic or cylindrical in shape (fig. 2). The parenchyma showed (a) a cortical substance, consisting of a much reduced stroma of small cells, the nucleus highly chromatic, displaying a wheelspoke formation, indicating the presence of atrophied interstitial cells; (b) a vascular-connective medullary substance. Not an intact follicle of any kind, no oocytes, no anovular formations, no tubular invagination of the epithelium was found. On the other hand, the parenchyma was riddled, as far as the medullary zone, with cavities, apparently of a cystic nature, containing structureless debris, strongly acid-fast, sometimes resembling a more or less wrinkled membrane: these were the remains, as yet unabsorbed, of large follicles which had degenerated as a result of the irradiation.

A similar histological examination was made of three ovaries, irradiated with 3,000 or 4,500 r, and opened from 106 to 149 days later. They presented the same appearance. There was some diminution in the number of recognizable interstitial cells; there still remained a large number of cavities indicating degenerated large follicles. There was no sign of repair or regeneration originating in the ovarian epithelium.

Finally, the ovaries of a mouse which had survived and remained sterile for 583 days after irradiation with 6,000 r showed an extreme degree of atrophy. Only the ovarian epithelium retained its characteristics. The internal structure of the organ was unrecognizable; cortical and medullary substance were indistinguishable; all traces of interstitial cells had disappeared. Moreover, there was now no trace of the cystic remains of the old unruptured follicles. The stump of the vascular-connective process showed what appeared to be several macrophages, containing a little pigment (fig. 3).

(3) *Atrophic lesions of the kidney.*—Our attention was attracted by a curious radiolesion, which, as far as I know, has not previously been described, and which sensibly modifies the classical theory as to the sensitivity of the kidney to irradiation. Possibly it may have escaped notice owing to the fact that it takes some time to establish itself. It was observed only in mice which had survived for longer than 300 days. There were four of these, three having received 3,000 and the fourth 6,000 r. All four presented the same changes.

It must be remembered that the ovary of the mouse is related to the inferior pole of the kidney; its irradiation accordingly involves a more or less important segment of the latter organ. On examining the body of a mouse irradiated only 340 days earlier, there was a marked deformation of the right kidney, which had become pear-shaped as a result of the atrophy of its lower half. In three other cases, where the subjects had survived for 570, 583 and 616 days respectively, the lesion was bilateral, being more marked sometimes on the right, sometimes on the left.



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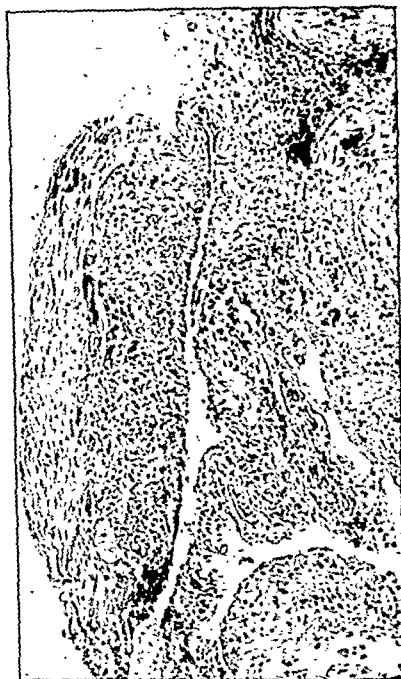


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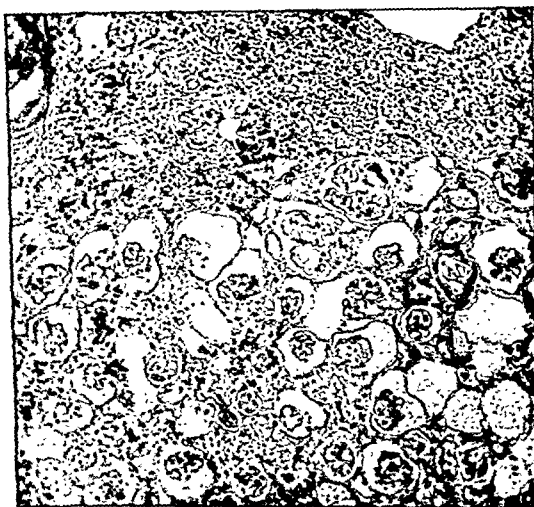


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it. I need not describe the cytolysis which may be observed by the end of the first twenty-four hours, and attacks simultaneously the epithelial cells of the epidermis and its invaginations, the endothelium of the capillaries and the connective cells of the dermis (fig. 5).

On the other hand, the process of repair is equally early and lively. As early as the third day, a layer of epithelial cells begins to migrate from the edges of the peripheral epidermis, producing a wedge-shaped penetration into the dead tissue; in the same way, from the fourth day onwards, mobile connective elements and new capillaries penetrate the dermis from all sides, and from the whole depth of the cutaneous muscle. By the seventh day, a new epidermis has grown under the disc of dead tissue which is about to separate in the form of a scab.

Moreover, in mice only a few days old, the healed epidermis retains the power to regenerate the sebaceous glands of the hair follicles. It develops on its deep surface buds which penetrate the dermis. But at this point most of them find themselves up against thick scar tissue, and so degenerate. Only a small proportion succeed in reaching the vascular plane formed under the cutaneous muscle and so become differentiated as sebaceous glands and hair follicles. This explains why the area once irradiated remains clearly recognizable, bearing only a few scattered hairs, and showing a slight depression owing to loss of substance and the atrophy suffered by the dermis (fig. 6).

(2) *In the adult mouse.*—As far as the absorption of the rays is concerned, the result seems to be identical with that in the newborn mouse. Necrosis is rapid, and attains the same depth of approximately 150 μ . But the much thicker skin of the adult mouse means that the rays work in different conditions, and so necrosis attacks only the epidermis and that part of the dermis immediately underlying it. Consequently, the sebaceous hair follicles suffer a kind of necrotic amputation below the neck, and only the upper half is destroyed (fig. 7).

As a result, the process of regeneration of the epidermis, which here also starts very early, is effected not only from the edges of the irradiated area, but also from the healthy stump of the epidermic sheaths of the hair. There is no formation of new follicles, but the preservation of a certain number of old ones—though many degenerate as a result of the sclerosis of the dermis in which they are rooted. Finally, after about twelve days, there is a cicatrix recognizable as a very slightly atrophied zone, sparsely sown with hair, closely resembling what I have described in the case of the newborn mice, but resulting from a somewhat different repair process.

(c) *Irradiation with L. Radiation of Silver.*

The experiments conducted with the collaboration of R. Latarjet, have not previously been the subject of a communication. They were all concerned with newborn mice. We set ourselves to discover the dose required in order to produce a destruction of the epidermis equal to that described above, and to compare the histolytic process and that of repair in the case of ultraviolet rays and X-rays.

We used a silver anode tube, functioning at 4,500 volts and 50 milliamperes. The distance between the window of the tube and the skin was not more than 1 mm. The rays were filtered by 15 μ of aluminium which gave a wavelength of about $4\frac{1}{2}$. In these conditions the absorption of the rays at various depths, according to measurements made by my collaborators Frilley and Latarjet, was 50% at 15 μ , 60% at 30 μ , 67% at 50 μ and 75% at 120 μ . Thus, with irradiation of different wave-lengths, we approximated closely to the limits of penetration previously observed when irradiating the skin of the mouse with ultraviolet rays.

Our first experiment was designed to establish the dose administered to the skin of the dorso-lumbar region, required to produce a lesion macroscopically comparable with that obtained with 1,500 f of ultraviolet rays. Eight young mice from the same litter were each given an increasing dose with a minimum of 44 and a maximum of 2,680 ergs per square millimetre. The successive reactions were noted, and it was apparent that the scabby ulceration obtained after the administration of 500 ergs gave place, once the scab had separated, to a partially hairless zone analogous to that described above in connection with irradiation by ultraviolet rays.

This dose was administered to eleven young mice from two litters which were killed after intervals of from three hours to nineteen days in order to provide material for the histological study of the establishment of the lesion and its repair.

The reactions apparent on direct examination of the skin of the living animal were much less rapid and severe than those caused by ultraviolet rays. There was erythema

A histological examination showed an unexpected feature of the area affected by the rays. The lesion did not involve the whole thickness of the organ, but decreased progressively. From the dorsal surface, where the rays had entered, it extended to a greater or lesser degree, actually, in some cases, reducing the transverse diameter of the kidney—which, in an adult mouse, is about five or six millimetres—by more than half. Under the thickened capsule were found, first a mass of malpighian bodies, almost in a state of fusion, among which all trace of the convoluted tubules had vanished. These corpuscles were in three, six or eight layers, according to the depth of the penetration. Nevertheless, among those which lay deepest the debris of uriniferous tubules could be seen:—isolated epithelial cells, or masses consisting of a few cells or hyaline casts—even tubules which had escaped necrosis sufficiently to be still recognizable as such. On the frontier between the lesion and the healthy renal parenchyma there was a definite and organized infiltration of leucocytes, sometimes forming quite a mass of lymphatic tissue surrounding the vessels.

But what is even more remarkable is the appearance of the malpighian bodies themselves. Whereas the epithelial covering of the uriniferous tubules was completely destroyed, the glomeruli were not affected and, as a rule, appeared to be intact. They were certainly still capable of functioning, for the capillaries contained red corpuscles, and the cavity was full of an acellular liquid, possibly slightly albuminous, since there was sometimes a little coagulum. But as this infiltrating liquid could find no way of escape, it distended the capsule, now reduced to a thin connective membrane. Each corpuscular cavity was thus dilated until its volume was at least doubled; the glomerular tuft being pushed back towards the vascular pole. In this state the irradiated area assumed somewhat the appearance of a polycystic kidney (fig. 4).

It would be interesting to establish, by experiments undertaken at an earlier stage, the successive stages of such lesions. This was not done. But the results described provide a conclusive argument in the age-long controversy as to whether parenchymatous lesions are the cause or the result of changes in the vessels. The uriniferous tubules here revealed quite clearly the extreme sensitivity to irradiation of the epithelial cells, presenting a remarkable contrast with the apparent integrity of the vascular formations.

(b) *Irradiation with Ultraviolet Rays.*

The various experiments now to be described were the subject of papers published by Lacassagne and Latarjet, in 1943 and 1945.¹ They allowed us to study the effects upon the skin, going as far as almost complete necrosis in newborn mice, only partial in adults, produced by strong doses of ultraviolet rays; and to note the process of repair.

The skin was irradiated in the dorso-lumbar region. The mice were protected from heat, and enclosed in a sleeve with an opening defining the required section of skin, usually bald, in newborn mice, and epilated a week earlier in adults. We used the total radiation of a Philips' Biosol mercury vapour lamp, calibrated in finsens per minute, 103.5 volts; 7.75 ampères, giving 300 f per minute. In these conditions we found that in mice one or two days old, the threshold value for erythema was 200 f, for true erythema 600 f, for desquamation 800 f; exudative epidermatitis was reached at 1,000 f, and necrotic dermatitis at 1,500 f, 90,000 ergs per square millimetre.

Let me describe the effect of this dose of 1,500 f upon an area measuring 6 by 5 millimetres in newborn mice, or 1 square centimetre in the adults.

(1) *In newborn mice* the irradiation in these conditions provokes, in the hours following administration, an enormous reaction producing œdema extending beyond the irradiated area, and accompanied by intense erythema lasting for five or six days. Then the affected area dries up and becomes covered with a scab, which separates after a week, revealing an epidermis, bald at first, but quite shortly to be sprinkled with scattered hairs.

Microscopical examination of the lesion thus produced in the skin of mice a day or two old reveals two things.

First there is a rapid local necrosis involving every variety of cell.

Secondly, this destruction is not deep-seated, but penetrates only to about 150 μ . Now in the case of these small immature animals the affected area includes the whole of the epidermis and the entire dermis, with the bulbs of the developing hair follicles buried in it. The destructive process reaches the cutaneous muscle without going beyond

¹C. R. Soc. de Biol. (1943), 147, 413 and 435; C. R. Soc. de Biol. (1945), 139, 4.

it. I need not describe the cytolysis which may be observed by the end of the first twenty-four hours, and attacks simultaneously the epithelial cells of the epidermis and its invaginations, the endothelium of the capillaries and the connective cells of the dermis (fig. 5).

On the other hand, the process of repair is equally early and lively. As early as the third day, a layer of epithelial cells begins to migrate from the edges of the peripheral epidermis, producing a wedge-shaped penetration into the dead tissue; in the same way, from the fourth day onwards, mobile connective elements and new capillaries penetrate the dermis from all sides, and from the whole depth of the cutaneous muscle. By the seventh day, a new epidermis has grown under the disc of dead tissue which is about to separate in the form of a scab.

Moreover, in mice only a few days old, the healed epidermis retains the power to regenerate the sebaceous glands of the hair follicles. It develops on its deep surface buds which penetrate the dermis. But at this point most of them find themselves up against thick scar tissue, and so degenerate. Only a small proportion succeed in reaching the vascular plane formed under the cutaneous muscle and so become differentiated as sebaceous glands and hair follicles. This explains why the area once irradiated remains clearly recognizable, bearing only a few scattered hairs, and showing a slight depression owing to loss of substance and the atrophy suffered by the dermis (fig. 6).

(2) *In the adult mouse.*—As far as the absorption of the rays is concerned, the result seems to be identical with that in the newborn mouse. Necrosis is rapid, and attains the same depth of approximately $150\ \mu$. But the much thicker skin of the adult mouse means that the rays work in different conditions, and so necrosis attacks only the epidermis and that part of the dermis immediately underlying it. Consequently, the sebaceous hair follicles suffer a kind of necrotic amputation below the neck, and only the upper half is destroyed (fig. 7).

As a result, the process of regeneration of the epidermis, which here also starts very early, is effected not only from the edges of the irradiated area, but also from the healthy stump of the epidermic sheaths of the hair. There is no formation of new follicles, but the preservation of a certain number of old ones—though many degenerate as a result of the sclerosis of the dermis in which they are rooted. Finally, after about twelve days, there is a cicatrix recognizable as a very slightly atrophied zone, sparsely sown with hair, closely resembling what I have described in the case of the newborn mice, but resulting from a somewhat different repair process.

(c) *Irradiation with L Radiation of Silver.*

The experiments conducted with the collaboration of R. Latarjet, have not previously been the subject of a communication. They were all concerned with newborn mice. We set ourselves to discover the dose required in order to produce a destruction of the epidermis equal to that described above, and to compare the histolytic process and that of repair in the case of ultraviolet rays and X-rays.

We used a silver anode tube, functioning at 4,500 volts and 50 milliamperes. The distance between the window of the tube and the skin was not more than 1 mm. The rays were filtered by $15\ \mu$ of aluminium which gave a wavelength of about 4Å . In these conditions the absorption of the rays at various depths, according to measurements made by my collaborators Frilley and Latarjet, was 50% at $15\ \mu$, 60% at $30\ \mu$, 67% at $50\ \mu$ and 75% at $120\ \mu$. Thus, with irradiation of different wave-lengths, we approximated closely to the limits of penetration previously observed when irradiating the skin of the mouse with ultraviolet rays.

Our first experiment was designed to establish the dose administered to the skin of the dorso-lumbar region, required to produce a lesion macroscopically comparable with that obtained with 1,500 f of ultraviolet rays. Eight young mice from the same litter were each given an increasing dose with a minimum of 44 and a maximum of 2,680 ergs per square millimetre. The successive reactions were noted, and it was apparent that the scabby ulceration obtained after the administration of 500 ergs gave place, once the scab had separated, to a partially hairless zone analogous to that described above in connection with irradiation by ultraviolet rays.

This dose was administered to eleven young mice from two litters which were killed after intervals of from three hours to nineteen days in order to provide material for the histological study of the establishment of the lesion and its repair.

The reactions apparent on direct examination of the skin of the living animal were much less rapid and severe than those caused by ultraviolet rays. There was erythema

on the third day, followed by pigmentation. On the eighth day, the irradiated area, still hairless, was the site of severe desquamation followed by superficial ulceration forming a scab on about the twelfth day, which separated on the sixteenth day exposing a red, smooth and hairless epidermis. The regrowth of hair began on the thirtieth day.

Nevertheless, histological study showed that cellular changes, although they began to declare themselves very early, affected only certain elements extremely sensitive to radiation. After twenty-four hours, this selective action of the rays was confined to the invaginations of the epidermis which were to constitute the hair follicles. Many of these cells already showed signs of advanced degeneration, whereas the epidermis, properly so-called, manifested no more than a simple cellular swelling and the disappearance of mitoses, and the dermis showed no reaction of the connective tissues. On the third day the epithelial lesions had become considerable; there was partial destruction of the follicle buds; the cells of the covering epidermis showed many anomalies and a general maturation of its elements gave the appearance of hyperkeratosis. Nevertheless there was no œdema of the connective tissue, simply a little diapedesis of leucocytes round the capillaries (fig. 8). The cornification of the whole epidermis and the degeneration of the follicular buds were very advanced on the fifth day, whereas there was only a slight infiltration of leucocytes in the immediately underlying dermis, and the deep layers were apparently unaffected. On the ninth day the progressive degeneration of the whole epidermis was complete; those parts which had cornified formed a scab beneath which a fresh layer of epidermis was beginning to creep in from the edges of the ulcerated area. There was marked inflammation of the dermis, with a strong infiltration of leucocytes, but no degeneration of the fixed cells (fig. 9). On the eleventh day, under the scab just about to separate, a thin, smooth epidermis had formed, which showed a few sparse invaginations.

This description of the histological process of degeneration of the epidermis by selective action on the cells of the germinative process agrees with the well-known account of epidermitis due to irradiation published by Regaud and Nogier; it is typical of the effects of X-rays in the shorter wave-lengths. On the other hand it differs completely from the diffuse necrosis of the epidermis caused by ultraviolet rays.

It might be supposed that this difference was due to the considerable inequality of energy applied in the two groups of experiments—9,000 ergs per square millimetre in the case of ultraviolet rays as against 500 for L radiations of silver,¹ in spite of the fact that these two doses resulted in an equal degree of macroscopic destruction.

Since in our search for the histological picture of skin lesions which should be comparable in one and the other of two types of radiation of different wave-lengths, an increase in the dose of X-rays would have been impossible, as it would have meant impossibly lengthy irradiation, the dose of ultraviolet rays had to be reduced.

Histological lesions produced by doses of 500 to 1,500 finsens.—Ten young mice from two litters of the same stock, two days old, were irradiated with a dose starting at 500 finsens, or 30,000 ergs per square millimetre, and increasing at each administration by 100 finsens. All the animals were killed three days later, just when the epidermic lesions would present their most characteristic appearance.

Even with a dose of 500 f, which, as mentioned above, caused only slight erythema, with no more serious desquamation than was found in the rest of the skin, and no loss of hair, the histological lesions were already obvious. But, unlike those caused by a dose of 1,500 f, they involved only a shallow depth of cells.

First, there was a squamous layer, thicker than the neighbouring integument, partly detached, and separated from the epidermis by a space containing a certain number of leucocytes, which had reached it by diapedesis through the remains of the epidermis, which, in fact, was not wholly destroyed. Here we recognized a picture resembling that described above in connexion with irradiation by 1,500 f of the thicker skin of the adult mouse: a continuous epidermis, forming a unicellular film in some parts, multistratified in others, including between the layers the follicular invaginations whose cellular elements were not attacked. The changes in the dermis consisted simply in the mobilization of the leucocytes; beneath the epidermis we found only a small number of cells which had undergone cytolysis (connective cells or leucocytes?). But there was obvious dilatation of the capillaries, the endothelium of which appeared to be intact; and there was a characteristic œdematous condition of the loose cellular tissue

¹It is important to remember that comparison of the results of irradiation by X-rays and ultraviolet rays on isolated cells (bacteria or ferments) has established that the same degree of lesion is obtained from the absorption of 200 times less energy in the case of X-rays than in that of ultraviolet rays (Latarjet, *Ann. Inst. Pasteur* (1913), 69, 205).

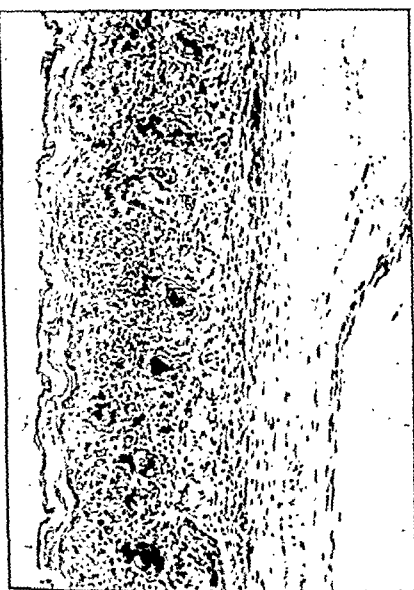


FIG. 6.—Irradiated skin of newborn mouse (ultraviolet radiation; dose 1,600 r) after 2 days. On left, irradiated segment; complete necrosis extending as far as the cutaneous muscle. On right, protected segment. $\times 25$.



FIG. 6.—Irradiated skin of newborn mouse (ultraviolet radiation; dose 1,600 r) after 12 days. On right, irradiated segment showing regeneration of the epidermis. On left, protected segment. $\times 25$.

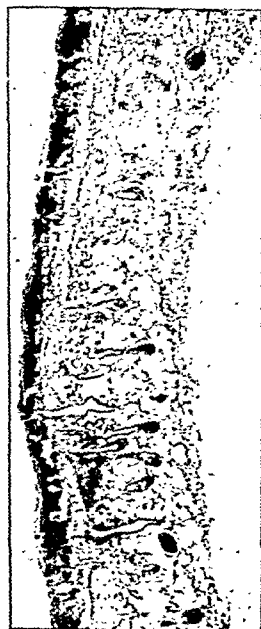


FIG. 7.—Irradiated skin of adult mouse (ultraviolet radiation; dose 1,500 r).

FIG. 8.

FIG. 8.—Irradiated skin of newborn mouse (L radiation of silver; dose 533 ergs/square millimetre) after 3 days. $\times 100$.



FIG. 9.—Irradiated skin of newborn mouse (L radiation of silver; dose 631 ergs/square millimetre) after 3 days. On right, irradiated segment. On left, protected segment. $\times 100$.

under the cutaneous layer. Moreover, the whole irradiated area was retarded in growth compared with the neighbouring areas. The dermis was thinner and the hair thinner and more sparse (fig. 10).

Here again there were none of the characteristics of an X-ray lesion of the epidermis, nor were there any after stronger doses; in fact, all that happened was that as the dose was increased the extension in depth of the diffuse necrosis increased in proportion. At 1,000 and 1,200 f this reached in the dermis about half the space between the epidermis and the cutaneous muscle.

We are thus forced to conclude that the destruction of the epidermis by ultraviolet rays and by X-rays is attained by two distinct histological processes. With ultraviolet rays there is no sign of selective radiosensitivity, but a kind of "all or nothing" effect, with necrosis of the cellular layers one after another, according as the increased dose



FIG. 10.—Irradiated skin of newborn mouse (ultraviolet radiation; dose 500 f) after 3 days. $\times 100$.

achieves the threshold value for cell destruction at greater and greater depth. X-rays, on the other hand, act selectively on the cells of the germinative layers of all the epithelial tissue, including the deep invaginations of the growing follicles.

SUMMARY

In conclusion, irradiation of a limited area of the dorsal lumbar region in mice was carried out with three types of radiation of different wave-lengths: K radiation of molybdenum, L radiation of silver and ultraviolet rays. Naturally deep-seated histological lesions, apart from those of the skin, were observed only in the first case.

(1) With a dose of K radiation of molybdenum, 3,000 r on the surface of the skin (corresponding to an incident energy of 760 ergs per square mm.) the only effect produced on the skin of the adult mouse is a clearly defined loss of hair, effected by selection, without ulceration of any kind. On the other hand, the ovary and parts of the kidney, situated about 5 mm. below the surface, are clearly and seriously affected. There is complete sterilization of the ovary and destruction of the uriniferous tubules, the glomeruli being unaffected. The fact that the intensity of the rays at a depth of 4 mm. is only about 25% of that on the surface makes it very clear that the epithelial tissues of the ovary and kidney are far more sensitive to irradiation than those of the epidermis.

(2) With L radiation of silver, a dose producing an incident energy of 500 ergs per square mm. applied to the skin of a newborn mouse causes destruction of the epidermis by a histological process of selective radio-epidermitis. The effect on the skin is thus much more severe than that caused by a stronger dose of K radiation of molybdenum. This difference is easily explained by the fact that the absorption of the rays by the skin is proportionately much higher in the case of the longer wave-length.

(3) Two radiations of different wave-lengths—L radiation of silver and ultraviolet rays—absorbed in depth in comparable proportions—both cause destruction of the skin of the newborn mouse, but the histological process in the two cases is totally different.

Section of Otology

President—A. J. WRIGHT, F.R.C.S.

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DISCUSSION ON THE CHEMOTHERAPY OF MENINGITIS SECONDARY TO INFECTION OF THE EAR AND NASAL SINUSES

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OTOGENIC meningitis and meningitis secondary to infection of the nasal sinuses have much in common. In both the bacteriology is similar, in both the meningitis may be complicated by abscess formation and in both the problems of treatment are in many respects the same. We therefore propose to discuss these two groups of cases together. We also include certain cases where the meningitis arose not from a frank sinusitis but as a result of a fracture involving the nasal sinuses (Table I).

TABLE I.—A SERIES OF 37 CASES SECONDARY TO INFECTION OF THE EAR AND NASAL SINUSES ANALYSED ACCORDING TO AETIOLOGY AND BACTERIOLOGY.

Source of infection	Pneumococci	Streptococci	Staphylococci	Mixed	<i>H. influenzae</i>	Total
Otitis	13	4	1	2*	1	21
Sinusitis	6	3	0	0	0	9
Fracture through sinuses	6	1	0	0	0	7
Total	25	8	1	2	1	37

* (i) Pneumococci + *Staph. aureus*; (ii) Streptococci + *Staph. aureus*.

Some of our patients were referred to us directly as cases of meningitis. Often this was because the bacteriologist who examined the C.S.F. identified Gram-positive organisms and made it his business immediately to get in touch with the clinician in charge of the case and urge treatment with penicillin. The site of the primary focus of infection was often discovered only after careful assessment of the history and clinical and radiographic examinations. Others were first admitted to hospital, either at Oxford or elsewhere, for treatment of the nose or throat. In these the meningitis usually developed while they were under observation. In those cases where the meningitis followed a fracture through the sinuses, some of the patients were admitted to hospital on account of their head injury, while in others the head injury preceded the meningitis by a variable interval and was only discovered by a study of the history.

From the practical point of view cases with this aetiology fall into three main groups: (1) Those in which no organisms are recovered from the C.S.F.; (2) those due to organisms which are either relatively or totally resistant to penicillin; (3) those due to infection by penicillin-sensitive organisms.

The first group includes those cases of relatively low-grade infection sometimes called "sterile" meningitis and also cases of intracranial abscess where bursts of mild meningitis develop during the course of the illness. These cases usually respond well to sulphonamides and unless an abscess is present no other form of chemotherapy may be needed. The patients must, however, be carefully watched and their progress checked by repeated bacteriological examination of the C.S.F., since fluid which is at first sterile may later give a positive culture (Smith *et al.*, 1946, Case 1). If the patient has received sulphadiazine before the lumbar puncture is done, cultures of the C.S.F. must be set up with para-aminobenzoic acid. They will otherwise probably be sterile when the true nature of the infection will be missed.

The second group is small but important. The predominating organisms are *H. influenzae* and *B. proteus*. Fortunately these cases are not common as the mortality in this country has been high. Occasionally influenza meningitis responds to heavy and prolonged dosage with sulphadiazine, while in America Alexander (1944) has achieved excellent results by the use of immune rabbit serum which is given in conjunction with sulphadiazine. Recently cases have been reported in which the infection has been controlled by intrathecal penicillin (Forgacs, Hutchinson and Rewell, 1945; Straker, 1945), and it appears that, at least with certain types, the resistance of *H. influenzae* to penicillin is relative rather than absolute.

We have treated one case of otogenic influenzal meningitis.

CASE I.—R.I. 25486/44.

A baby of 8 months was one day noticed to have a thick purulent discharge coming from his right ear. He did not seem unwell at that time but five days later the left ear also began to discharge. Eight days later he was admitted to the Ear, Nose and Throat Department of the Radcliffe Infirmary, and the following day a bilateral Schwartz mastoidectomy was performed. The right mastoid contained a fair amount of mucopus, but the left only showed some injection. Following operation the condition of his ears was uniformly satisfactory, but his temperature rose, and he was given sulphathiazole (3 grammes daily). For the next ten days his temperature was maintained at about 102° F. without the development of any physical signs, but on the eleventh day he developed a squint and on the twelfth day was found to have considerable neck stiffness. A lumbar puncture revealed a cloudy fluid but no organisms were seen on the direct film, and it was not until four days later that the organism grown on culture was identified as *H. influenzae*.

During these four days, treatment with intramuscular and intrathecal penicillin was given in view of the previous lack of improvement on sulphathiazole. There was no clinical improvement throughout this period.

When the organism was reported as insensitive to penicillin, sulphadiazine (3 grammes daily) was begun, and the penicillin discontinued. Thereafter the child slowly improved, but one attempt to reduce the dose of sulphadiazine, and another to discontinue the drug after three weeks, were quickly followed by clinical and bacteriological relapse. Finally the child made a complete recovery after having received sulphadiazine for seven weeks. At no time were any signs of drug intolerance detected.

The third group is the largest and most important. The commonest organisms are pneumococci and streptococci, both hæmolytic and anaerobic. Staphylococci are much rarer (Stewart, 1929; Weinstein, 1942). The predominance of pneumococcal over streptococcal infections in our series may be due to the fact that we were making a special study of pneumococcal meningitis at the time when these cases were treated; on the other hand, before the days of effective chemotherapy, many cases of pneumococcal meningitis must have died before admission to hospital. Our experience is still very limited, especially with streptococcal and staphylococcal meningitis, but we will produce evidence that the nature of the organisms is of considerable practical importance. The bacteriology and aetiology of cases is shown in Table I. We have omitted those cases where the nature of the organisms was not proved by culture.

Except for meningococcal meningitis, which seldom requires treatment with penicillin, the treatment of meningitis due to penicillin-sensitive organisms is essentially the same whatever the infecting organism. This may conveniently be considered under three headings: (1) Treatment of the leptomeningitis; (2) detection and treatment of a complicating intracranial abscess; (3) treatment of the primary focus of infection.

(1) Treatment of Leptomeningitis

We have recently described our methods in full (Smith *et al.*, 1946) but the most important points in what we consider the basic treatment of meningitis may be recapitulated. As a routine we use both intrathecal and systemic penicillin with sulphadiazine by mouth. Penicillin for intrathecal use is made up in a solution of 2,000 u./c.c. and given in doses of from 8,000 to 10,000 units. During the first thirty-six to forty-eight hours injections should be given every twelve hours but thereafter daily injections are usually sufficient. The efficacy of dosage and treatment should be checked by daily bacteriological examination of the C.S.F. and estimation of its penicillin content, which, in a few patients, reveals that penicillin escapes unusually quickly from the C.S.F. In these the frequency of injections can then be increased so that a bacteriostatic concentration is constantly maintained.

The easiest and safest way of giving the intrathecal injections is by lumbar puncture. About 6 c.c. of C.S.F. is withdrawn for examination, and the penicillin then slowly injected. The injection should be frequently interrupted by aspiration of C.S.F. This insures that the needle is correctly placed and also dilutes and warms the solution. The lumbar route is only effective when the cerebrospinal pathways are patent. The earliest sign of their occlusion is a slowing in the flow of C.S.F. and difficulty in aspiration during the injection. This observation must be checked by repeating the tap in a higher space and using a wide-bore needle since if it is confirmed it is an absolute indication for giving penicillin either by the cisternal or, preferably, by the ventricular route.

The intrathecal penicillin is supplemented by the oral administration of sulphonamides. Sulphadiazine, in doses of 12 grammes in twenty-four hours, is at present the preparation of choice because it diffuses freely from the blood into the C.S.F. It therefore reaches all parts of the cerebrospinal pathways including any loculi that may be inaccessible to the penicillin. It is given to suppress the virulence of the infection and thus to help maintain the patency of the cerebrospinal pathways. In any case of

meningitis treatment with sulphadiazine should be begun immediately as this will tide the patient over the interval that may elapse before treatment with penicillin is started. Systemic penicillin is given either by continuous intramuscular drip or by intermittent three-hourly injections. The minimal daily dose is 120,000 u. in twenty-four hours, but in certain cases, for example in the presence of a frank septicæmia, this should be increased as much as 320,000 in twenty-four hours. We have no evidence that systemic penicillin alone can cure meningitis and its chief value lies in the control of the primary focus of infection and of a complicating septicæmia or pyæmia.

The intrathecal penicillin must be continued for at least five days, for although clinical and bacteriological improvement is usually obvious after three days, the cerebrospinal fluid has probably not been completely sterilized. 10 of the 37 patients in this series relapsed even after a full intrathecal course, and from our experience, if less than five days' treatment is given the proportion that relapse increases. There is also the danger that the relapse may be fatal and uncontrollable. Relapse is most common within the first forty-eight hours after the last intrathecal injection but may occur even while the patient is receiving daily lumbar injections. When this happens, either the solution in use has lost its activity, or penicillin is not reaching the site of infection, or is escaping from the theca unusually rapidly. Two of our patients relapsed even when convalescence seemed assured, and in two others isolated positive cultures from the C.S.F. were obtained without any concomitant clinical disturbance. Sulphadiazine should be given during the period in which the intrathecal penicillin is withdrawn as it provides a safeguard against uncontrollable relapse.

In a relapse, rise in temperature and recrudescence of headache and malaise precede the reappearance of cells and organisms in the C.S.F. by as much as twenty-four hours. The treatment of relapse does not differ from that of the initial attack and in our experience the prognosis as regards life and functional recovery is not altered, provided that each relapse is promptly recognized and treated. We would emphasize the need for vigilance and persistence in treating the severe relapsing case, as a complete cure can be obtained even when the illness lasts over three months.

Relapse may be due to inadequate treatment or to reinfection of the meninges either from the primary focus or from a small intrathecal fibrino-purulent collection. In otogenic cases, is relapse an indication for opening the mastoid? In only one of our cases did this prove necessary.

CASE II.—R.I. 5657/44. *Reinfection from the primary focus* (Smith *et al.*, 1946, Case VI).

A bricklayer aged 53 had a right mastoidectomy performed elsewhere following a six weeks' history of severe earache. The immediate post-operative course was smooth except that he developed a complete facial palsy, but ten days after operation he vomited, his temperature rose and he developed signs of meningitis. Lumbar puncture was performed and pneumococci (Type III) were grown on culture from the C.S.F. Treatment with sulphathiazole was at once begun and two days later he was transferred to Oxford. On admission his general condition was excellent and except for the complete right facial palsy there were no abnormal neurological signs. The mastoidectomy wound was healed and the ear was dry. Lumbar puncture revealed an almost clear C.S.F. containing only 160 cells but pneumococci were once more grown on culture.

He was then treated with intrathecal penicillin and sulphadiazine but systemic penicillin was withheld. His progress was uneventful but eight days after his last intrathecal injection he relapsed and cultures of the C.S.F. again became positive. He received a further course of intrathecal penicillin and sulphadiazine and again responded well. During convalescence he was seen by Mr. Livingstone who advised re-exploration of the mastoid and a facial nerve graft.

At operation it was found that the original operation had been incomplete. Mr. Livingstone's note states: "The antrum had never actually been reached. There were many mildly infected cells over the dura and lateral sinus. When the residual cells were removed, the sinus was found to be healthy, but in one place the dura of the middle fossa was covered with rough granulations, and these were thought to be the route of the entry of his meningeal infection". Cultures taken from this patch of granulations grew pneumococci.

The facial nerve was then freed from all residual cells and the defect repaired by a graft.

He made a permanent recovery from his meningitis and when seen a year later was free from symptoms except for a moderate right-sided deafness of middle-ear type. There was satisfactory recovery of the facial palsy.

The meninges more often become reinfected from a small intrathecal fibrino-purulent collection as in the following case:

CASE III.—*Reinfection from an intrathecal fibrino-purulent collection* (Smith *et al.*, 1946, Case VII).

A regular soldier aged 39 developed pneumococcal meningitis secondary to a right-sided otitis media. Both the initial attack and a relapse were controlled by sulphapyridine but following the second attack he died from an inhalation bronchopneumonia.

Examination of the brain revealed a collection of pus within the right auditory nerve which was continuous with a tiny abscess in the right lateral recess of the fourth ventricle (fig. 1).

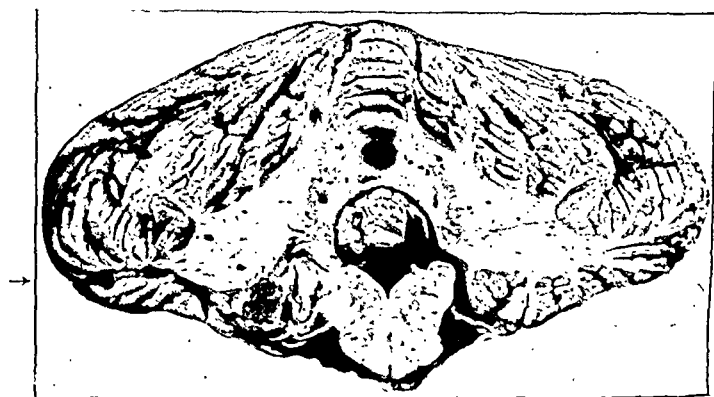


FIG. 1. (Case III).—Section through medulla and cerebellum showing a fibrino-purulent collection within the sheath of the right eighth nerve continuous with a small abscess in the right lateral recess of the fourth ventricle (arrows). Such fibrino-purulent collections are probably the commonest cause of relapses.

Two of our patients whose meningitis was not primarily otogenic in origin developed a nerve type of deafness during the course of this illness. This deafness is presumably analogous to that so often seen in the past in meningococcal meningitis. In one of these patients at least, we presume the lesion was similar to that just described (fig. 1) as her illness ran a prolonged relapsing course before she ultimately recovered.

CASE IV.—R.I. 36553/44.

The patient, a housewife of 52, was admitted as an emergency on the medical side on October 24, 1945. About four weeks earlier she had caught a cold in the head and had had a slight cough but this had not interfered with her normal activities. At 8 o'clock the evening before her admission she had been visited by her daughter-in-law, who noticed no signs of ill-health, but during the night she vomited and became drowsy though restless. By the following morning she was semicomatose with neck stiffness and photophobia and with a temperature of 102°F. She was forthwith sent to hospital.

On admission she was extremely ill. She was stuporous but any attempt at examination provoked outbursts of silent struggling. Her neck was very stiff and Kernig's sign was positive. There were unequivocal signs of consolidation at the base of the right lung. Lumbar puncture showed an unusually purulent fluid (25,000 cells per c.mm.) which was swarming with pneumococci. Blood culture was also strongly positive.

Treatment was begun with intrathecal and intramuscular penicillin and sulphadiazine, but by the same evening the flow of C.S.F. was so sluggish that bifrontal burrholes were made and an intraventricular injection of penicillin given. Thereafter she steadily improved but on recovering consciousness was found to be deaf in the right ear and to have rapid poorly sustained nystagmus on looking to the left. She was also retentive of urine, and both ankle-jerks were absent.

On the eleventh day, while she was still receiving daily lumbar injections of penicillin, her temperature which had previously fallen, rose suddenly to 103°F.; she complained of headache and her neck was again stiff. Lumbar puncture the same evening showed the cells of the C.S.F. had risen from 66 to 2,500 in ten hours. The frequency of the intrathecal injections was increased, and her symptoms subsided. This was the first of seven relapses, most of which followed attempts to withhold intrathecal penicillin. No focal signs were ever detected except the right-sided deafness with nystagmus and the mild cauda equina syndrome. There was never any discharge from the ear and Mr. Macbeth, who saw the patient on several occasions, only found evidence of a transient otitis media and pan-sinusitis. He considered this part of her initial respiratory infection, and in no way responsible for the relapses and that there was therefore no indication for operation.

Unlike our other relapsing cases, in this case each relapse was milder than its predecessor and none was comparable in severity to the initial attack. The last relapse was treated with sulphamezathine only, as she had developed an intolerance to sulphadiazine (Total: sulphadiazine—136 grammes, sulphamezathine—141 grammes). Following this, recovery was permanent and she has now no residua from her long and trying illness except a moderate right-sided deafness of inner-ear type. The whole illness lasted thirteen weeks.

This case presents several points of interest:

(a) The C.S.F. at the onset of the illness was exceptionally purulent (25,000 cells/c.mm. and over 1,000 mg. of protein/c.c.). As might be expected under those conditions, a cerebrospinal block threatened to develop during the first twenty-four hours of her illness. This necessitated an intraventricular injection of penicillin. The following day the signs of incipient block had disappeared, and treatment could be continued by the lumbar route.

(b) A mild cauda equina syndrome developed during the first thirty-six hours of the illness and recovered after eight weeks. Both this and the nerve deafness were probably

due to the deposition of fibrino-purulent material round the nerve roots, as there was no correlation between the appearance and disappearance of the symptoms, and the lumbar administration of penicillin.

(c) During an illness lasting thirteen weeks the patient relapsed seven times. The earlier and more severe of these occurred while lumbar penicillin was already being given and were treated by increasing the frequency of the intrathecal injections. The later and milder relapses followed attempts to withhold intrathecal penicillin and were treated by giving a further course of injections, until the last which was successfully treated with sulphamezathine alone.

(d) Finally, this case illustrates the reversal in prognosis. Before the introduction of chemotherapy pneumococcal pneumonia complicated by septicæmia and meningitis was a lethal disease (Osler's Textbook of Medicine, 1937). Now, with penicillin and sulphonamides, full recovery can be achieved.

Precautions in use of penicillin intrathecally.—Treatment with intrathecal penicillin is not without its dangers. Of the four chief-risks three are common to all cases of meningitis while the fourth is particularly apposite in those cases which follow infection of the ear or nose.

(1) The brand of penicillin must be suitable for intrathecal use. As soon as a non-irritating preparation has been secured it should be set aside for treatment of meningitis. The best at present available is crystalline penicillin 2 (Glaxo Ltd.).

(2) Excessive dosage (40,000 u. or over at a single dose), especially when concentrated solutions are used, is capable of producing severe cerebral reactions, or, when given by lumbar puncture, damage to the cauda equina or gumming of the subarachnoid space. This last is particularly unfortunate as the most convenient route of access is then no longer available.

(3) There is a very definite risk of introducing secondary infection, especially when frequent relapses demand a large number of injections. For this reason the penicillin solution should be put in small quantities and each container only used once. A strict aseptic technique in preparation of solutions and in lumbar puncture is imperative.

(4) There is a danger in doing repeated lumbar taps on any patient with high intracranial pressure. This is probably negligible except when the meningitis is complicated by an abscess, when it is considerable. This combination of meningitis and abscess is particularly common in cases secondary to infection of the ears or nose.

Finally the closest observation and the best of nursing care are essential to success (Smith, Day and Welch, 1946). "You may hope to push the patient through, but to do so you must watch him hour by hour" (Watson, 1848).

(2) *The Detection and Treatment of a Complicating Intracranial Abscess*

Intracranial abscess and leptomeningitis are both well-known complications of otitis and sinusitis, and each has its own distinct symptomatology. Formerly we knew of cases where a cerebellar abscess was complicated by meningitis, and of others where a terminal meningitis and ventriculitis arose as a complication of abscess of the cerebral hemispheres. But since we have been treating meningitis with penicillin we have met cases in which meningitis and intracranial abscess appear to develop together. The clinical picture may then be so dominated by the signs of meningitis that the abscess is not suspected until the patient, instead of making the expected response to intrathecal penicillin, becomes moribund from raised intracranial pressure.

CASE V.—R.I. 25905/44.

The patient, a child of 12, came under our care in the early days of penicillin therapy and before we were aware of this particular combination of abscess and meningitis. Thirteen days before she had been admitted to hospital elsewhere with an acute infection of the ethmoid and sphenoidal sinuses complicated by an orbital cellulitis. She was treated with sulphathiazole in doses of 6 grammes in twenty-four hours. The infection persisted and on several occasions she vomited and complained of headache. After twelve days the ethmoid sinuses were curetted and the same evening she developed signs of meningitis. Lumbar puncture yielded a turbid fluid in which streptococci were identified and the day after operation the child was transferred to Oxford.

On admission she was delirious and extremely ill, with marked meningeal signs. There were no focal signs except right-sided proptosis. Lumbar puncture was performed. The C.S.F. was purulent and the pressure well above 300 mm. of water. 25 c.c. were withdrawn and 10,000 u. penicillin in 10 c.c. injected. After the needle was withdrawn, C.S.F. leaked through the skin puncture for several minutes in spite of firm pressure. Following lumbar puncture she rapidly grew worse and four hours later she died. Autopsy revealed a large abscess occupying the right frontal pole.

We have now seen 8 such cases of simultaneous abscess and meningitis: 4 were otogenic and 4 followed pan-sinusitis. Of the latter 4, in 3 there was a history of severe, acute sinusitis, while in the fourth the intracranial infection followed a chronic sinusitis with osteitis of the skull. In 2 there were signs of orbital cellulitis. Of the otogenic cases, in one no adequate history could be obtained; in one there was a six weeks'

history of earache, the tympanic membrane was very thick and scarred with a small anterior attic perforation and offensive purulent discharge; in the third there was a definite history of previous attacks of otitis; and in the fourth the abscess developed in a pre-existing brain fungus. It is thus possible that the abscess really predates the meningitis, although clinically they appear to develop simultaneously. The clinical detection of a complicating abscess may be extremely difficult especially as in none of our cases was any definite papilloedema detected.

In our experience the most important clue in diagnosis is the bacteriology of the infection. In our 26 cases of pneumococcal meningitis secondary to ear and nose infections, only 2 were complicated by an abscess. By contrast, among 9 cases of streptococcal meningitis an abscess was present in 5. An abscess was also found in our one case of otogenic staphylococcal meningitis. This same correlation between the bacteriology and abscess formation is seen in our cases of meningitis from other sources (fig. 2).

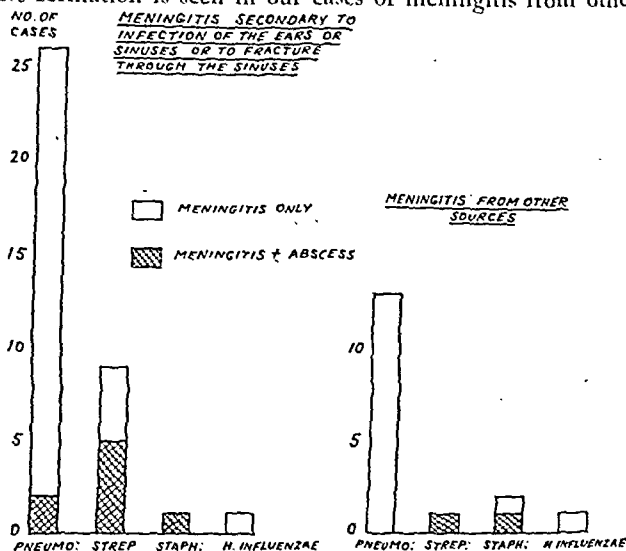


FIG. 2.—The incidence of a complicating intracranial abscess in the different bacteriological varieties of meningitis both in the cases forming the present series and in those of meningitis from other sources.

The type of streptococcus was not determined in every case, but there is some indication that abscess is commonest in the anaerobic streptococcal infections (Cairns and Schiller, to be published). The abscess may be intracerebral or subdural or both, but wherever it is its detection is imperative since not only does the abscess itself demand prompt surgical treatment but the meningitis must be treated by intraventricular penicillin instead of by the routine lumbar injections. Owing largely to the difficulties in diagnosis we have not yet succeeded in saving any of our otogenic cases of simultaneous meningitis and abscess. We have, however, been successful in two cases secondary to sinusitis.

CASE VI.—R.I. Illustrating the diagnostic problem of simultaneous meningitis and abscess.

A storekeeper of 47 was admitted to hospital as an emergency under the care of Mr. Livingstone. For the past fifteen years he had suffered from intermittent attacks of mild right-sided earache associated with a thin, watery discharge. Ten days before admission, the pain and otorrhoea returned, but later the discharge ceased and the pain became much worse. Twenty-four hours before admission he had a rigor and his temperature rose steeply.

On admission he was in considerable pain from his ear, his neck was a little stiff, and his temperature just over 100°F. The right external auditory meatus was filled with thick pus. Lumbar puncture revealed a cloudy fluid under a pressure of 240 mm. of water. No organisms were seen on the films and cultures were sterile. Treatment with sulphadiazine was begun, and a few hours later a right radical mastoidectomy was performed, and an extradural abscess opened. The middle fossa was widely exposed until healthy dura was found. The wound was closed with drainage.

Following operation he steadily improved and nine days later began getting up. In the early hours of the tenth day the symptoms of meningitis returned with increased severity. The C.S.F. was found to be frankly purulent and to contain a number of streptococci. By 2.30 p.m. he was delirious and very ill with gross meningeal signs. No definite focal signs could be discovered on neurological examination. Treatment with intramuscular and intrathecal penicillin was begun but the lumbar C.S.F. was now so thick and the flow so sluggish that intraventricular injections were indicated. Accordingly bifrontal burrholes were made and the left lateral ventricle tapped. Here the pressure

was found to be 500 mm. of water and about 30 c.c. of purulent fluid were withdrawn. The right ventricle was only found with difficulty and appeared collapsed. In the light of later experiences this finding should have been interpreted as indicative of an abscess but this was the first of our cases of simultaneous abscess and meningitis, nor were we aware at that time of the prevalence of abscess in streptococcal infections. An intra-ventricular injection of penicillin was therefore given and nothing further was done. The patient died quite suddenly about six hours after operation, and autopsy revealed, in addition to the leptomeningitis, a large subdural collection of pus overlying the right temporal lobe and in relation to the dura over the tegmen tympani.

In order to detect this difficult group of cases the procedure should be as follows:

As soon as meningitis is suspected in a patient who has well-marked signs of otitis or sinusitis he or his relatives should be questioned as to previous attacks and the patient then carefully examined for focal signs. A lumbar puncture is then cautiously performed, the initial pressure of the C.S.F. is measured and 4 to 5 c.c. slowly withdrawn. Cultures are set up and a Gram-stained film immediately examined. If pneumococci are recognized, and the C.S.F. is running freely, a lumbar injection of penicillin is given and the patient treated on the lines already described. If, however, streptococci are seen, an intracranial abscess should at once be suspected, and suspicion is greatly strengthened if the C.S.F. pressure is far in excess of 300 mm. of water or if focal signs have been elicited.¹ A lumbar injection of penicillin may be given at the time of the diagnostic tap, but the presence of an abscess must then be confirmed or excluded by ventricular estimation or ventriculography, since penicillin makes ventriculography safe even in the presence of an active infection.

If no abscess is found the meningitis is treated in exactly the same way as pneumococcal meningitis. The sensitivity of the organism to penicillin should be assessed as some strains of streptococci are relatively resistant. Nevertheless we have not yet needed to exceed our usual range of dosage.

If an abscess is found it must be dealt with surgically in order to prevent a fatal rise in intracranial pressure.

Cerebral abscess.—If the rise in pressure is due to the actual accumulation of pus, rather than to oedema, the abscess should be aspirated and penicillin is then instilled into the abscess cavity. Thorotrast may be injected at the same time, as it does not inactivate penicillin and facilitates subsequent management (Pennybacker, 1945). A more concentrated solution of penicillin is indicated for instillation into an abscess cavity than is advisable for intrathecal injections, and we use a solution of 10,000 u/c.c. as opposed to our standard intrathecal solution of 2,000 u/c.c. The exact amount will to some extent depend on the size of the abscess cavity, but is usually 1 to 3 c.c. If there is abundant pus, aspiration will be enough to control the rise in pressure, but if only a small quantity can be aspirated, the intracranial pressure must be controlled by ventricular taps or drainage. If this too fails the patient will require a decompression over the abscess, as unless the rise in pressure is relieved he will die; but in the presence of meningitis wide opening of the dura should be avoided if possible since the raised intracranial pressure will produce great herniation with corresponding increase in destruction of the brain (Falconer and Russell, 1944; Holbourn, 1944).

Subdural abscess.—A subdural collection of pus is dealt with by the insertion of fine rubber catheters through suitably placed burrholes. Through these catheters, which are left open, pus is aspirated and penicillin instilled. The subdural space does not retain penicillin like the subarachnoid, and four- to six-hourly injections are therefore needed. The number of burrholes required varies, but in one of our successful cases no fewer than five had to be made in order to ensure access to the whole of the subdural collection. When the limits of the subdural abscess have been defined, two further burrholes should be made through which the intraventricular penicillin can be given without passing the brain needle through the infected area.

The concomitant lepto-meningitis is controlled by intraventricular injections of penicillin. These are begun when the diagnostic ventricular tap is performed and continued either by intermittent taps or, if the ventricle is being drained, by instillation through the catheter. The same scale and frequency of dosage is used as with lumbar injections, but unless the intracranial pressure has been adequately lowered by aspiration of the abscess or other means no attempt must be made to treat the meningitis by the lumbar or cisternal route. These are not only useless but highly dangerous. The pressure of the abscess distorts the subarachnoid channels at the tentorial opening and elsewhere, and may prevent the penicillin from reaching the ventricles or spreading upwards over the hemisphere (Cairns, Duthie, Lewin and Smith, 1944). Moreover a lumbar or cisternal puncture carries a very real risk of producing a fatal pressure cone, nor is this risk lessened by an injection of penicillin.

¹Focal signs do not always indicate an abscess, but may be caused by cerebral thrombophlebitis. Thus in one of the cases in this series the patient developed a left hemiplegia and left homonymous hemianopia. Abscess was excluded by ventriculography. The whole of the intrathecal penicillin was given by lumbar injection, and recovery was complete.

history of earache, the tympanic membrane was very thick and scarred with a small anterior attic perforation and offensive purulent discharge; in the third there was a definite history of previous attacks of otitis; and in the fourth the abscess developed in a pre-existing brain fungus. It is thus possible that the abscess really predates the meningitis, although clinically they appear to develop simultaneously. The clinical detection of a complicating abscess may be extremely difficult especially as in none of our cases was any definite papilloedema detected.

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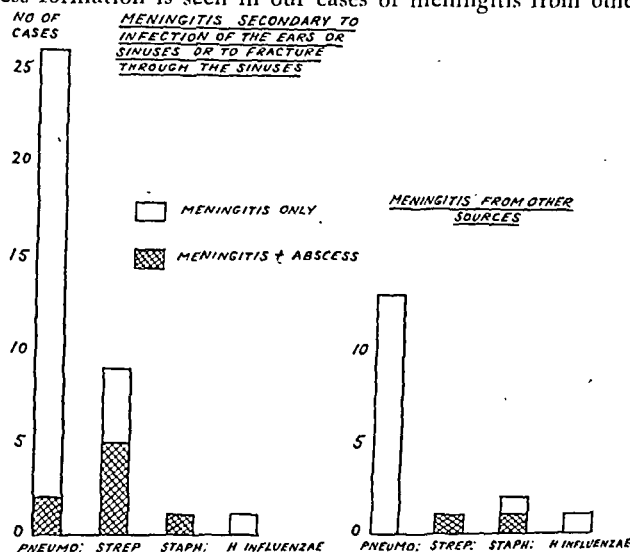


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By 5.30 p.m. he was desperately ill: there was pronounced head retraction, he was cyanosed, and his respirations which had risen to 40 per minute were interrupted by bursts of hyperpnoea when the rate would rise to 60 or even 70. He was mute and restless and any interference provoked paroxysms of violent but silent struggling. There was a right facial weakness of lower motor neurone type, but no other focal signs. Lumbar puncture yielded turbid fluid under a pressure of over 300 mm. of water and an examination of a smear of C.S.F. showed Gram-positive diplococci. *Pneumococcus* Type 14 was grown on culture.

At 7 p.m., when he came under our care, he seemed in extremis. At this stage treatment was begun with intrathecal and intramuscular injections of penicillin. At 8 p.m. he was seen by Mr. Livingstone who advised against further operation on the ear.

During the next twenty-four hours there was little change in his general condition except that the rapid deterioration ceased. X-rays taken of his mastoids showed evidence of an acute mastoiditis on the right side. Twenty-four hours after treatment with penicillin was begun his temperature fell, and thereafter his recovery was rapid and complete. During his illness he was again seen several times by Mr. Livingstone who was fully satisfied with the progress of the ear. When discharged from hospital, all the clinical and radiological evidence of infection had disappeared. When last seen, two years after the meningitis, there had been no recurrence of symptoms in the right ear, though a few weeks before this he had a mild attack of left-sided otitis media.

Thirteen patients had no operation. As soon as supplies of penicillin were adequate, all received from 120,000 to 320,000 u. daily by intramuscular injection, in addition to their intrathecal penicillin and oral sulphadiazine. This was continued until the active infection had subsided. Although there were four fatalities, in no case would the outcome have been altered by operation on the ear. One infant died a few hours after treatment was begun; here delay in instituting chemotherapy was the decisive factor. Two died from intracranial abscess and one from acute cerebral oedema. In the other 9 cases not only was recovery from the meningitis complete but there has been no return of the aural symptoms. Mr. Macbeth and Mr. Livingstone have seen most of these patients and, except in one (Case II), they have not advised operation. Only 2 of these 9 cases relapsed, and in both the intrathecal course of penicillin had been incomplete. The following case is an example of control of the primary focus without operation.

CASE VIII.—R.I. 20891/44.

The patient, a schoolboy of 11, had always been a backward child. Three years earlier he had begun to suffer from recurrent attacks of right-sided otitis. From time to time he would complain of earache, then after a few days the ear would begin to discharge and the pain would cease. On May 14, 1944, he developed a cold in the head and a purulent discharge from the right ear. Fourteen days later he complained of headache, grew drowsy and restless, and his parents noticed that his head was retracted. These symptoms all steadily increased and after five days he was admitted to hospital elsewhere. A lumbar puncture was performed and hæmolytic streptococci grown from the C.S.F. Treatment with sulphathiazole was begun and the following day he was transferred to Oxford.

Examination at that time showed an ill, wasted child with spina bifida, but no cauda equina symptoms. He was semiconscious and at times would scream with pain from the intensity of his headache. Head retraction and opisthotonus were so marked that he had considerable difficulty in swallowing. Upward movement of the eyes was limited but no other focal signs were found on neurological examination. There was no mastoid tenderness but thick offensive pus, from which a *Staphylococcus aureus* was cultured, was welling through a perforation in the right tympanic membrane. X-rays of the mastoids taken three days later showed sclerotic bone with a few small cells and an opaque antrum.

Treatment with sulphadiazine and intramuscular penicillin was begun immediately. In view of the possibility of a complicating brain abscess, the lateral ventricles were tapped through frontal burrholes. Both were found to be dilated which made the presence of an abscess unlikely. On culture, *Staphylococcus aureus* was grown from the ventricular and *B. hæmolytic streptococcus* from the lumbar fluids. Intrathecal penicillin was given by ventricular and lumbar injections and he made a slow but satisfactory recovery from his meningitis.

Mr. Macbeth saw this patient in acute phase of the illness and in view of our past experiences he thought it justifiable to await developments before advising operation. This course was fully justified by subsequent events. Six days later the perforation had healed and by the time the meningitis was fully controlled Mr. Macbeth declared himself satisfied with the ear. Follow-up studies during the subsequent eighteen months showed recovery both from the meningitis and the otitis to be complete.

Two patients were operated on during convalescence. The first was the patient on whom complete mastoidectomy was performed some weeks after a relapse of the meningitis (Case II). The second was a girl of 14 who developed an acute right-sided mastoiditis two months after she had apparently made a complete recovery from an attack of pneumococcal meningitis secondary to a mild right otitis media. Mastoidectomy was performed elsewhere, and a pure culture of *Staphylococcus aureus* grown from the pus. Though the relation between the original otitis media and the mastoiditis is therefore uncertain, operation early in convalescence would have prevented the second attack.

Our successful cases in which no mastoidectomy was performed include examples of chronic otitis as well as of recurrent (Cases VII and VIII) and acute otitis. In every case the

In those cases of streptococcal meningitis where the patient's general condition is good, when there are no focal signs, or clinical evidence of an excessive rise in intracranial pressure, and where the C.S.F. pressure is under 300 mm. of water, it is probably justifiable to institute treatment by the lumbar route, provided the patient is closely watched for signs of rising intracranial pressure and provided also that full facilities exist for immediate ventricular puncture should the need arise. Even so an abscess may be missed. We have had 2 patients who fulfilled the above criteria and yet were later shown to have a small abscess. The danger signals are a progressive rise or fall in the pulse-rate, periodic respiration, and an increase in stupor. The need for constant observation cannot be exaggerated, and while the possibility of abscess exists these cases really demand the whole of the surgeon's time and attention.

Our experience with staphylococcal meningitis is very limited, but the fact that 2 out of our 3 cases have been complicated by abscess suggests that staphylococcal and streptococcal meningitis present similar problems.

(3) Treatment of the Primary Focus of Infection

Since the time of Gowers (1888) immediate surgical drainage of the primary focus of infection has generally been considered axiomatic in the treatment of otogenic meningitis. Valuable as sulphonamides are in the treatment of meningitis, opinion is still divided as to whether or not they have lessened the need for immediate operation on the primary focus. Thus Watkyn-Thomas (1941) defined the principles of treatment as: (1) Elimination of the primary focus; (2) drainage of the subarachnoid space; (3) appropriate counter-medication.

Now that penicillin is available the place of operation in treatment should be reassessed by otologists, and in this connexion our experiences in conjunction with our otological colleagues may be of interest. Our series of 21 cases of otogenic meningitis has been analysed according to the incidence and time of operation, the history, the recovery rate and cause of death (Table II).

TABLE II.—TWENTY-ONE CASES OF OTOGENIC MENINGITIS SHOWING THE TIME-RELATION OF OPERATION ON THE EAR TO THE COURSE OF THE ILLNESS, THE PREVIOUS HISTORY, THE RESULT AND THE CAUSE OF DEATH.

Operation	No. of cases	Previous otitis	Recovered	Died	Cause of death
Mastoidectomy before meningitis ...	3	2	2	1	Abscess
Mastoidectomy at height of meningitis ...	3	1 (?)	2	1	Heart failure and inhalation pneumonia
Myringotomy at height of meningitis ...	1	1	1	0	—
Mastoidectomy during convalescence ...	2	1	2	0	—
No operation...	13	4	9	4	(i) Delay in chemotherapy, (ii and iii) abscess, (iv) acute cerebral oedema

One patient (Case II) had two operations. Previous otitis = a previous history of infection of the ear.

In 3 cases mastoidectomy failed to prevent the development of meningitis several days later, though in one the operation was admittedly incomplete. It is possible that a prophylactic course of systemic penicillin, given either alone or with sulphonamides, over the period of operation might prevent the development of meningitis in such cases, since a protective action has been claimed for sulphonamides alone (Weinstein, 1942).

Three patients had been operated upon at the height of the meningitis before they came under our care. In the 2 who recovered mastoidectomy preceded the institution of penicillin therapy by three days and three weeks respectively. In neither had it had any apparent effect on the meningitis which was already partially controlled by sulphonamides. In the fatal case mastoidectomy was performed immediately before penicillin therapy was begun. The patient had a stormy time during operation; he stopped breathing, and was with difficulty resuscitated. The following day he developed heart failure and died. A severe inhalation pneumonia was found at autopsy.

The single case in which an emergency myringotomy was done was one of fulminating pneumococcal meningitis.

CASE VII.—R.I. 23632/44 (Falconer *et al.*, 1946. Case III).

The patient, a schoolboy of 15, had an attack of right-sided otitis media in December 1943. This responded well to sulphonamides and he returned to school the following term. At 4 p.m. on April 14, 1944, he had a recurrence of his earache and his temperature rose to 102.5°F. The ear was examined, and though the tympanic membrane was reddened no indication for operation was found. He was given 2 grammes of sulphadiazine and thereafter received 1 gramme every four hours. Next morning at 4 a.m. he awoke complaining of headache and vomited, by 11.30 a.m. he was delirious and had considerable neck rigidity; the tympanic membrane was bulging. He was transferred to a nursing home where at 2.30 p.m. a myringotomy was performed and a fair quantity of pus released without any effect on his general condition. Since he was by now unable to swallow the sulphadiazine was continued by intramuscular injection.

difference in the prognosis is apparent when the causes of death are considered (fig. 5). A complicating abscess is the commonest cause of death, and the combination of abscess and meningitis is most common in streptococcal infections. In our 6 fatal cases of pneumococcal meningitis, in 2 only was death due to abscess formation. Three patients died from delay in instituting chemotherapy, and 1, a traumatic case, from fat embolism while recovering from his meningitis. Although we have not yet been fortunate enough to cure a patient in whom meningitis and abscess followed disease of the ear, our successes with cases secondary to sinusitis encourage us in the belief that no patient is too ill to recover with chemotherapy and suitable surgical intervention.

SUMMARY

Otogenic meningitis and meningitis secondary to infection of the nasal sinuses are considered together, since the problems of treatment are similar. Such cases fall into three main groups: (1) Those in which no organisms are recovered from the C.S.F.; (2) those due to organisms which are relatively or totally resistant to penicillin; (3) those due to penicillin-sensitive organisms.

A series of 37 cases (Table I), of which all but one fall into the third group, is described. The predominating organisms were pneumococci and streptococci.

The basic treatment of purulent meningitis with penicillin is briefly recapitulated, the mechanism of relapse discussed, and the hazards associated with the administration of penicillin intrathecally are pointed out.

Eight cases have been encountered in which the meningitis was complicated by an intracranial abscess. Diagnosis of the abscess is difficult, since both abscess and meningitis appeared to develop simultaneously, but its detection and immediate treatment are imperative. This combination of abscess and meningitis is seen most often in streptococcal infections. In our total series, out of 38 cases of pneumococcal meningitis, only 2 were complicated by an abscess, while out of 10 streptococcal cases, a concomitant abscess was present in 6.

The treatment of the primary focus of infection is discussed since the use of systemic penicillin demands reassessment of the place of emergency mastoidectomy in the treatment of otogenic meningitis. In 21 otogenic cases with 15 recoveries only 2 patients had a mastoidectomy at the height of the meningitis; 13 patients had no operation on the ear, and of these 9 recovered completely from both the meningitis and the otitis. In none of the fatal cases could mastoidectomy have saved the patient's life, and, in fact, operation with general anaesthesia may tip the scales against the patient when performed at the height of an attack of meningitis. Whether operation is still necessary once the meningitis has been controlled is a matter which must be decided by the otologist.

In the present series of cases the results with pneumococcal have been better than with streptococcal meningitis owing to the frequency with which the latter disease has been complicated by intracranial abscess.

Finally we would like to thank our colleagues, Mr. Macbeth and Mr. Livingstone, for allowing us to treat their cases, and for the help they have given us with our own cases.

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Mr. J. Eric Paterson: My observations are based on material treated in the Neurosurgical Unit at Killearn Hospital, near Glasgow. The Unit was established four years ago, and the material includes therefore cases treated before and after the advent of penicillin. It is selected material; most of the cases have been referred, either from an otologist or from a fever hospital, because progress was unsatisfactory, because some such complication as brain abscess was feared, or because it was felt that penicillin administration by some special route, such as into the ventricle, should be carried out.

In our penicillin cases we have had only 6 patients with uncomplicated otic menin-

case with which the initial attack of meningitis was controlled was approximately the same. Nor did the 6 patients who had had a mastoidectomy done before they came under our care respond better to treatment than those who had not. In fact, in 1 fatal case the stress of anaesthesia and operation at the height of the meningitis probably prejudiced the patient's chance of recovery.

Though we have thus no evidence that operation is of value in treatment of the acute phase of the meningitis, it sometimes has a place in the treatment of the relapsing case. That the meninges can be reinfected from the primary focus is certain (Case II), but what is not known is how frequently this occurs. Evidence is accumulating that reinfection from an intrathecal fibrino-purulent collection (Case III) is the commoner mechanism. During treatment of a case of meningitis, whether otogenic or secondary to sinusitis, in which relapse follows relapse, the idea of an active primary, extrathecal focus which is constantly reinfected the meninges is very difficult to resist. Nevertheless, in our experience, attempts to stop relapse by operative treatment of extradural sources of infection have been disappointing.

Whether early operation is necessary in order to preserve hearing is not a matter for us to decide. It is, however, interesting that while several of our patients have been slightly deaf on first recovering consciousness, in only 2 has this been permanent. In neither case was the meningitis otogenic and in both the deafness was of nerve type.

Our experience with penicillin thus suggests that mastoidectomy need no longer be performed as an emergency in cases of otitic meningitis. In this connexion it is interesting that work done on experimental pneumococcal infections in animals shows that general anaesthesia (alcohol, ether and avertin) inhibits the activity of the leucocytes and allows the organisms several hours in which to multiply unchecked (Pickrell, 1938).

Once the meningitis has been cured, whether mastoidectomy is still required, and whether this depends on the chronicity of the otitis, are questions which must be answered by the otologist. It is likely that the answer may be most easily found from study of cases of otitis uncomplicated by meningitis. It is, however, clear from the observations made by our otological colleagues on cases in this series that, at least in the acute case, full recovery can be attained by systemic chemotherapy. In any case, the patient is dying not from the mastoiditis but from his meningitis. Prompt and adequate treatment of the meningitis must therefore take precedence over other therapeutic measures.

The treatment of acute sinusitis is less debatable. Adequate doses of penicillin can control the infection, even when this is complicated by frank osteitis of the skull. Even if this becomes reactivated after withdrawal of the systemic penicillin it can be dealt with at leisure after the meningitis is controlled.

When meningitis follows a fracture through the sinuses with tearing of the dura, the dural defect should be repaired as soon as the patient has recovered from his meningitis (Cairns, 1937). Similar treatment is not so often required for fracture of the petrous bone with tear of the overlying dura.

RESULTS

In our 37 cases there have been 26 recoveries and 11 deaths (fig. 3). Up to the present time the prognosis has usually been considered best in cases of streptococcal and worst

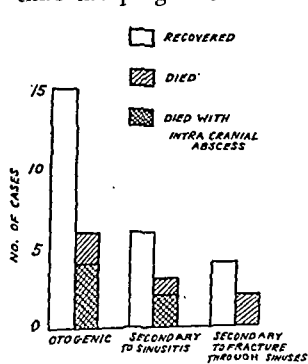


FIG. 3.—Classification of the results according to the mode of primary infection.

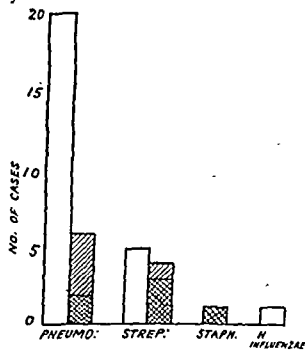


FIG. 4.—Bacteriological classification of results.

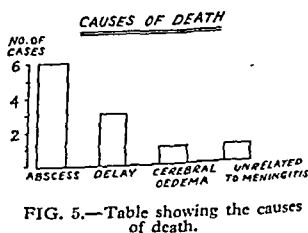


FIG. 5.—Table showing the causes of death.

in cases of pneumococcal meningitis (Hutchison, 1942; Weinstein, 1942). Our results are very different. Out of 26 cases of pneumococcal meningitis, 20 recovered, while out of 9 cases of streptococcal meningitis, only 5 recovered (fig. 4). The reason for this

difference in the prognosis is apparent when the causes of death are considered (fig. 5). A complicating abscess is the commonest cause of death, and the combination of abscess and meningitis is most common in streptococcal infections. In our 6 fatal cases of pneumococcal meningitis, in 2 only was death due to abscess formation. Three patients died from delay in instituting chemotherapy, and 1, a traumatic case, from fat embolism while recovering from his meningitis. Although we have not yet been fortunate enough to cure a patient in whom meningitis and abscess followed disease of the ear, our successes with cases secondary to sinusitis encourage us in the belief that no patient is too ill to recover with chemotherapy and suitable surgical intervention.

SUMMARY

Otogenic meningitis and meningitis secondary to infection of the nasal sinuses are considered together, since the problems of treatment are similar. Such cases fall into three main groups: (1) Those in which no organisms are recovered from the C.S.F.; (2) those due to organisms which are relatively or totally resistant to penicillin; (3) those due to penicillin-sensitive organisms.

A series of 37 cases (Table I), of which all but one fall into the third group, is described. The predominating organisms were pneumococci and streptococci.

The basic treatment of purulent meningitis with penicillin is briefly recapitulated, the mechanism of relapse discussed, and the hazards associated with the administration of penicillin intrathecally are pointed out.

Eight cases have been encountered in which the meningitis was complicated by an intracranial abscess. Diagnosis of the abscess is difficult, since both abscess and meningitis appeared to develop simultaneously, but its detection and immediate treatment are imperative. This combination of abscess and meningitis is seen most often in streptococcal infections. In our total series, out of 38 cases of pneumococcal meningitis, only 2 were complicated by an abscess, while out of 10 streptococcal cases, a concomitant abscess was present in 6.

The treatment of the primary focus of infection is discussed since the use of systemic penicillin demands reassessment of the place of emergency mastoidectomy in the treatment of otogenic meningitis. In 21 otogenic cases with 15 recoveries only 2 patients had a mastoidectomy at the height of the meningitis; 13 patients had no operation on the ear, and of these 9 recovered completely from both the meningitis and the otitis. In none of the fatal cases could mastoidectomy have saved the patient's life, and, in fact, operation with general anaesthesia may tip the scales against the patient when performed at the height of an attack of meningitis. Whether operation is still necessary once the meningitis has been controlled is a matter which must be decided by the otologist.

In the present series of cases the results with pneumococcal have been better than with streptococcal meningitis owing to the frequency with which the latter disease has been complicated by intracranial abscess.

Finally we would like to thank our colleagues, Mr. Macbeth and Mr. Livingstone, for allowing us to treat their cases, and for the help they have given us with our own cases.

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Mr. J. Eric Paterson: My observations are based on material treated in the Neuro-surgical Unit at Killearn Hospital, near Glasgow. The Unit was established four years ago, and the material includes therefore cases treated before and after the advent of penicillin. It is selected material; most of the cases have been referred, either from an otologist or from a fever hospital, because progress was unsatisfactory, because some such complication as brain abscess was feared, or because it was felt that penicillin administration by some special route, such as into the ventricle, should be carried out. In our penicillin cases we have had only 6 patients with uncomplicated otitic menin-

gitis, that is, unassociated with other intracranial lesions such as brain abscess. Two of the 6 cases died, both had been sent in late.

The sulphonamides in acute otitic meningitis.—We give a course of sulphonamide in every case in very large doses. Until recently we used sulphamezathine, since with this drug the risk of renal complications is very small; but since Kremer, Phillips and Stanier (1945) showed that it was most difficult to obtain with it an effective concentration in the cerebrospinal fluid we have used sulphadiazine, with which the concentration has been shown to reach 60 to 80% of the blood level. We have not yet experienced renal crystallization or agranulocytosis. We give a dose of 5 grammes and continue with 3 grammes four-hourly for the first twenty-four hours, followed by 2 grammes four-hourly for a week, when we allow one to two days to elapse without sulphonamide before beginning another such course, if this is thought advisable. When a sulphonamide is used alone—and it must not be forgotten that meningitis may result from a penicillin-resistant organism—the risk of sulphonamide poisoning must be balanced against the risk of a fatal ending in these grave cases. Following the lead of Mr. Norman Dott we have deliberately taken this risk. I know of one patient in whom, over a period of three weeks, a total of 318 grammes was administered, with final recovery; that is, an average dose of $2\frac{1}{2}$ grammes every four hours throughout.

There were some excellent results in pre-penicillin days in streptococcal infections. One case of chronic otitis media which sustained a fracture through the petrous bone had acute meningitis with pus under the temporal fascia. Recovery was rapid after sulphonamide administration and a mastoid operation.

Penicillin therapy.—Our intrathecal doses have hitherto been generally not more than 40,000 units daily, but I shall increase the dosage in the light of what has been said, particularly now that the drug is available in an increasingly pure form. Penicillin reactions have occurred in a few of our cases: several patients complained of pain in the feet, which disappeared when the intrathecal injections were stopped. This we ascribed to an irritation of the cauda equina. Two cases ran a mild temperature, which fell at once to normal when the drug was withdrawn.

Intraventricular penicillin is given when there are signs of a cerebrospinal fluid block, but patients with obstructive hydrocephalus, sent to the neurosurgeon late, do badly; treatment must be prophylactic, early. For instance, a girl of 8 was admitted from a fever hospital. She had papilloedema, bilateral sixth and right seventh nerve palsies. Ventriculograms showed a large hydrocephalus; the fourth ventricle was dilated, but the gas had failed to pass into the cisterna magna or forward along the base. She died sixteen days after admission; intrathecal, intraventricular and systemic penicillin was powerless to deal with the obstruction at the foramina of Luschka and Magendie.

But these foramina are small in size, and there are cases where, in the absence of signs of cerebrospinal fluid block, penicillin given intrathecally may be much less effective than when given by the ventricle. We have only very recently begun to estimate the cerebrospinal fluid bacteriostatic level, but the result is not available immediately, and it would seem wise to begin ventricular administration as soon as the sample of fluid has been taken, without waiting for the result. Here is a case which illustrates the importance of giving intraventricular penicillin in the apparent absence of obstruction. A girl of 7 was admitted a week after an acute head injury. There were a cerebrospinal fluid otorrhoea and a staphylococcal meningitis. Under systemic and intrathecal penicillin she continued to run a temperature for three weeks, with varying, but often high, cerebrospinal fluid cell-count, while her general state deteriorated. Finally, when the count rose to 2,400, ventriculography was done. This disclosed ventricles which were normal in size, without any evidence of obstruction throughout the cerebrospinal fluid pathways. Intraventricular penicillin was started at once and the temperature fell to normal two days later; recovery was uneventful.

Reaction to intraventricular penicillin.—Johnson and Earl Walker (1945) describe the case of a boy of 22 months who was given a dose of 50,000 units by this route. He became unconscious and so collapsed that his blood-pressure could not be estimated. Three hours later he had a generalized convulsion, and this latter was repeated, without loss of consciousness, when he was given another injection three days later. In the case of the little girl just described there was likewise a considerable degree of collapse, without any convulsion; fortunately this is the only example we have had in our series. It is to be anticipated that such disturbances will become less frequent as the drug becomes available in purer form.

Cisternal penicillin.—Little need be said about administration into the cisterna magna. Its place must be very limited indeed. Speaking as a neurosurgeon, I know I should

much rather inject the drug into a ventricle than try to tap a cisterna magna in a child with pronounced opisthotonos. However, I have notes of one case of pneumococcal infection in which a spinal block developed, and which made an excellent recovery with intracisternal penicillin.

Systemic penicillin.—Systemic administration is a most important part of the treatment of these cases; the difficulty is to know how long to continue the drug by this route; usually we play for safety and continue possibly longer than we need to. But we must not exaggerate the efficacy of systemic penicillin in acute meningitis or agree with Reese (1944) when he states that intrathecal penicillin is never necessary, since the drug is excreted into the cerebrospinal fluid in bacteriostatic concentration when the choroid plexuses are rendered more permeable by the disease. As the work of Professor Cairns and his associates has shown, in pneumococcal meningitis only traces of penicillin appear in the cerebrospinal fluid after the systemic injection of even very large doses.

I agree with Professor Cairns that operation on the infected ear should not be carried out in the acute phase of the meningeal infection before this is under control. In systemic penicillin we have a most potent weapon in the control of the spread of the infection from the primary focus to the meninges, and we must exploit it to the full. Operation under general anaesthesia may well turn the scale against recovery; and operation under local anaesthesia must be extremely difficult in a restless, delirious patient. But reinfection of the meninges may readily occur, and if operation is indicated it should be carried out as soon as acute infection has been overcome, while the patient is still on his initial course of systemic penicillin.

Rigid asepsis in intrathecal and intraventricular administration is of extreme importance.—In the past three years I have treated three cases of staphylococcal meningitis following lumbar puncture. Two of these followed spinal anaesthesia, and there were two deaths in this small series.

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Mr. R. G. Macbeth said that Dr. Honor Smith and Professor Cairns had asked him to comment on the otological aspect of their communication. It was obvious that with the coming of penicillin therapy otologists must accept a greatly changed outlook on the question of when or even whether they should open mastoids in the presence of otogenic meningitis. One thing which did emerge was that the mastoid operation need no longer be a matter of great urgency. One could safely delay doing a mastoid operation until the meningitis was under control, and the patient therefore more fit for operation.

In acute cases it seemed necessary only to do the simplest operation productive of drainage of the middle-ear cleft. Where the ear was discharging already, no operation might be needed; where there was no discharge, a myringotomy might suffice. Penicillin did not sterilize pus inside an abscess cavity, but it would aid the resolution of an inflammatory process within a draining middle-ear cleft. A patient who had an extradural abscess in the middle or posterior fossa was an exception to that rule, and it was probable that one could get a hint about such a case from careful attention to clinical signs. For example, such a patient might complain of persistent pain and tenderness behind the ear in spite of adequate chemotherapy, and continue to have otorrhœa and cells in the cerebrospinal fluid.

Relapsing cases of meningitis seemed to be commoner with nasal-sinus infections than with mastoiditis, as one would expect from a consideration of the connexions between the nasal sinuses and the subarachnoid space.

It seemed likely that operation would be called for in almost every case of meningitis due to chronic otitis. It was difficult to imagine that a sufficiently high concentration of penicillin could be delivered to deal with the primary focus in chronic bony disease.

Mr. T. B. Layton said that no distinction had been made in the paper presented by Dr. Honor Smith between chronic ear disease and acute inflammations of the middle-ear cleft. In every paper dealing with an otological subject that distinction must be made. The two diseases were as distinct clinically, bacteriologically, and therefore pathologically, and in their response to treatment, as were acute peritonitis and tuberculous peritonitis.

He disagreed with Mr. Paterson that it might become unnecessary to operate on the acute ear, but that operation had still to be done on the chronic ear. He had made the planned experiment of refraining from operating in meningitis of an acute ear because he thought that a condition of the heart was the dominating lesion which would forbid a general anæsthetic to be given. The patient came out of the meningitis but relapsed. He then had operated, but the patient died. He would find it a very grave responsibility to refrain from removing that factory of organisms which was down against the dura mater. There was a distinct difference in disease of the ear and the sinuses. One was a disease of bone, contiguous with which was the periosteum—the dura mater, and therefore the spread from one to the other was easy and rapid; the other was an inflammation of a mucous membrane separated from the cranial cavity by two layers of periosteum and an intervening piece of bone, and all one could do was to drain that cavity, if one knew exactly from which of the half dozen or so channels it was spreading through to the meninges.

Mr. E. Musgrave Woodman said that those working so extensively on penicillin were to be congratulated on the change that had taken place in the prognosis of pneumococcal meningitis. He had always been taught that pneumococcal meningitis was an incurable disease.

Why was it that penicillin seemed so impotent to control a migrating streptococcal abscess in the brain?

As to whether they should operate on an acute mastoid which was accompanied by meningitis or brain abscess, they had all been taught that the primary focus should be removed when consequential complications arose. But these patients were very ill, their margin of safety was low, and a little thing would tip them over the border. In the best interests of the patient it might be that a simple drainage without eradication should be carried out.

Mr. C. P. Wilson said that probably those cases which developed symptoms associated with a cerebral abscess were more likely to go to a neurosurgical unit than to an otologist. In his 8 cases of otitic meningitis there had been only one death. That was in a pneumococcal case. 3 cases had grown a hæmolytic streptococcus which had been recovered.

Intrathecal dosage.—He had discussed this with Professor McIntosh, pathologist, Middlesex Hospital. Originally these cases were given 2,000 units per c.c. intrathecally according to the amount of cerebrospinal fluid removed, but lately they had been as much as 50,000 units in otitic and non-otitic cases. He queried this amount, Professor McIntosh, because he felt it was much more likely to produce a reaction with fibrinous exudate, but Professor McIntosh's opinion was that often had fibrinous exudate without penicillin, and he (Professor McIntosh) had often had the amount of exudate was not greater with penicillin, but it was not serious. In this series they had had only two complications: paralysis of the median nerve which was now recovering, and a case of *petit mal*. Thus the disadvantage of using very large doses intrathecally did not seem to have been particularly borne out in Professor McIntosh's experience at Stoke.

Mr. L. Graham Brown said that four months ago he had a case of a flare-up on a chronic infection. He carried out a complete mastoidectomy. The patient did very well for three weeks and then developed a facial palsy. The wound and cleaned up the infection still present. Since the palsy continued he carried out a cerebrospinal examination and found abscess. He called in a neurologist, who, however, could not locate anything. The patient was put upon sulphonamide treatment and penicillin systemically. Very well, the wound healed up completely, the temperature fell, and the patient returned to the hospital. A month later, however, he returned with further palsy. He (Mr. Graham Brown) suspected suffering from a sphenoidal abscess, but his hand was stayed by the fact that the patient was ready to operate, but before any further information could be obtained he died. At post-mortem a temporosphenoidal abscess was found.

This case was interesting from the point of view of the relation between the otologist and the neurosurgeon and neurologist. It was obvious

a little difficulty in carrying out completely all those difficult tests and treatments which the neurosurgeon was now making his own. He desired to ask Professor Cairns if he did not agree that, in those cases where brain abscess or an intracranial complication was suspected accompanying meningitis, the neurosurgeon should take charge. He was one of those otologists who thought that these cases were really getting beyond their range of full responsibility.

Mr. Terence Cawthorne said that a contribution from outside was always welcome at that Section particularly when it carried with it the experience of the Neurosurgical Department at Oxford. Penicillin had quite clearly altered in some respects their views of otogenic meningitis. He desired to ask whether there was any likelihood of systemic penicillin being able to be a substitute for intrathecal medication. These constant lumbar punctures were a source of trouble and possibly a danger. He had seen two cases of meningitis secondary to lumbar puncture, both in cases in which spinal anaesthesia was carried out, and the organism in each case was *B. pyocyaneus*.

Mr. Layton's very forcible exposition of the importance of differentiating between acute and chronic otitis media would command general agreement. They were two quite different diseases when it came to the management of an otogenic meningitis. On the question of draining a primary focus it might be asked, what was a primary focus? Meningitis following rapidly upon an otitis media was a mucous membrane disease not a bone disease, and the infecting focus could not be eradicated by carrying out wide surgical excision of bone. This only made it easier for infection to spread even further. The meningitis which followed within hours or days upon an otitis media should be dealt with conservatively.

Meningitis following upon a long-standing otitis media was a different matter. He had in the past said that he thought such cases should be operated on without delay, but he now felt that it was wiser to give chemotherapy and the antibiotics a day or two's start before operation. He had no doubt that in cases of intracranial complications of chronic suppurative otitis media the best way of getting a good result was by intimate co-operation between the otologist, the neurologist and the neurosurgeon.

Mr. F. W. Watkyn-Thomas said that to control meningitis by any chemotherapeutic method, sulphonamide or penicillin, they must have an agent which would penetrate the perivascular sheath, pass along the vessels, and percolate the brain substance. The sulphonamides passed the choroid plexus, entered the ventricles and passed, by the perivascular spaces, through the brain. Was there evidence that penicillin, unless administered by the intraventricular route, would do that? To what extent would intrathecal penicillin do anything except pass over the outer surfaces and eventually be absorbed? Would it actually enter the brain substance? He knew that theoretically it was possible to get a reverse current of the cerebrospinal fluid, but was there any evidence that that occurred in penicillin administration? He was deeply impressed, but not quite convinced by Dr. Honor Smith's paper, and he did not think that he was going to abandon the removal of the focus when there was one. Later on he might be converted.

Mr. H. V. Forster said that only a few days ago he had been asked to examine a man who had recovered from acute purulent meningitis associated with a history of inflammation in one ear. Intrathecal and systemic penicillin had been successfully given.

At his, Mr. Forster's, examination, the middle-ear disturbance was found to have subsided and the drumhead to be intact.

In earlier days before sulpha and penicillin therapy, one expected to see few cases recover from meningitis, complicating an acute primary otitis media.

In acute inflammation of the middle-ear cleft, he had always felt that early drainage through its bony walls should be withheld and would like to support Mr. Cawthorne's views on the pathology of this type of infection.

In chronic otitis media with an exacerbation, complicated by meningitis of markedly purulent type, it had not been unusual in earlier days to see recovery after eradication of the primary focus of disease, assisted by lumbar puncture. Perhaps a certain degree of immunity had been developed through the years of chronic infection. In such cases, the possibility of a complicating brain abscess would confront the otologist who need not fear to explore for it with the serum needle and a syringe to provide suction to draw off the pus. He had great confidence that if the abscess cavity were entered by the needle, pus would not refuse to be drawn into the barrel of the syringe. He did not think that to explore through the roof of the operation cavity in this way gave any serious

risk of infecting healthy brain tissue and the resulting instrumental trauma was not greater than that following the puncture in ventriculography.

Fatal cases of otitic brain abscess followed to the post-mortem room rarely showed an undrained loculus but a condition of spreading encephalitis.

Was there any evidence to show that penicillin was able to control the advance of the encephalitis?

The President said that this interesting discussion could be summed up by saying that certainly penicillin did hold out the hope of helping cases which were hopeless in the past. It had also demonstrated the need for co-operation between the otologist and the neurosurgical units, and they were very grateful to Oxford for setting such an outstanding example of this.

Professor Hugh Cairns, who replied on the Discussion, said this subject had reached a stage at which the pathology of the primary focus had become of urgent clinical interest. The use of modern antibiotics in any field of pathology raised individual problems peculiar to that field, and the question of the infection of the mastoid and petrous bone was no exception to this rule. Neurosurgeons and other people working at Oxford had been drawn closer to the otologist over the use of penicillin than they had ever been before. He thought particularly of the cases of pneumococcal meningitis where relapse occurred. The patient got cured of one attack of pneumococcal meningitis and then got another, and this sequence might go on for months, and they found themselves badgering their otological colleagues to come and tell them whether there was a primary focus in the ear which was still active and whether it ought to be operated on, rather hoping that they would say "Yes." That was just one example of the type of thing with which they were now confronted.

The dosage of intrathecal penicillin.—They were very much against large doses; the standard dosage intrathecally should be about ten thousand units in one dose. It might be given twice a day in the very acute phase of the meningitis, but for most of the time it was sufficient to give it once a day. Excessive doses could cause trouble—fits, retention of urine, and other symptoms of damage to the cauda equina. Furthermore, all the available evidence went to show that excessive dosage was unnecessary. With the dosage recommended a concentration of penicillin in the cerebrospinal fluid would be obtained which was more than ample to destroy any of the ordinary pathogenic bacteria like pneumococci or streptococci.

Intrathecal treatment must be systematic, and the least time for intrathecal treatment in a proved case of pathogenic meningitis was five days. Often it was desirable to go on for rather longer.

What penicillin could do prophylactically, both for infection at the mastoid and infection at the brain, had yet to be proved. Mr. Watkyn-Thomas put a fundamental point when he asked whether the penicillin could diffuse into the brain from the capillaries. The answer was that nobody knew, and it was an extremely difficult problem to work at experimentally. It was known that, given systemically, the penicillin would not pass in any appreciable amount into the theca. It was also known that patients who were given penicillin systemically in adequate doses would still have relapses of meningitis. Therefore, in answer to Mr. Cawthorne's question, he did not think there was any likelihood, with the present compounds, that systemic treatment would replace intrathecal treatment.

If Mr. Layton would read the opening paper he would find that they had in fact distinguished between the acute and the chronic cases. A chronic focus, where there was a collection of pus or sequestra, ought to be dealt with surgically. However, he was not clear from what had been said whether Mr. Layton would hold his hand in any case or whether he would go ahead and operate on all of them, acute and chronic, as he did in the old days. As far as osteomyelitis of the long bones was concerned surgeons had changed their views very considerably since the advent of penicillin.

Patients who got an attack of pneumococcal meningitis did not seem to become more immune, at any rate not for a long time. Relapses, of which there might be eight or nine in one case, were just as severe as the initial attack. If each attack of meningitis were treated as patiently and energetically as the first, and the surgeon in charge did not lose heart or allow the nurses to lose heart, success would be achieved and the patient would in the end cease to relapse.

There was a great field here for the otologist to work out precisely the degree to which penicillin could help him in the treatment of mastoid infection and also in its prevention in cases of otitis media.

Section of the History of Medicine

President—Sir ARTHUR MACNALT, K.C.B., M.D.

[May 1, 1946]

Phthisis in the Seventeenth Century

Growth and Development of Knowledge¹

By Professor S. LYLE CUMMINS, C.B., C.M.G.

THE early part of the seventeenth century marks the beginning of a great expansion of experiment and fact in medicine in general and in the treatment of tuberculosis in particular. The domination of thought by the ancient observations of Hippocrates (460 B.C.) and of Galen (A.D. 131-200) was giving way before the results of research and growing points of positive knowledge were apparent on all sides. Noteworthy among these was the discovery of the "lesser" or "pulmonary" circulation of Realdus Columbus (1510-1599) of Cremona. "The blood", he says, "goes through the vena arteriosa to the lungs; then, mixed with the air, it goes through the arteria venosa to the left heart" (Guthrie, *Hist. Med.*, 1945). But the mightiest step forward in medical research was the discovery of the complete circulation of the blood through the whole body, activated by the motion of the heart, demonstrated by William Harvey (1574-1657) in 1616 and, after complete verification, published by him in his great work, *De Motu Cordis* in 1628. The first English work on phthisis to which I have so far had access is the *Theatri Tabidorum Vestibulum* of Christopher Bennet (1617-1655). This author was born when Harvey was 39 years old and at the prime and fruition of his work; a year after he had made his great discovery and eleven years before he gave it, in its published form, to the world. It is a feature in medical research that great discoveries, duly published, have a galvanizing effect on medical thought. Christopher Bennet, as a graduate of Oxford, must have been aware of Harvey's work though not, perhaps, as appreciative of its importance as we are to-day. His theory of the development of a phthisis or consumption of the lungs may or may not be founded on it. "From this Incitement of the Blood", he says, "which, for the most part, is the Efficient of Secretion, and from the Expression of Serum from the lungs, moderately be-dewing them, a frequent spitting will sometimes be raised; but if a Person is overflowed with a great Profusion of such Serosities which induce a general Laxity, a more protracted Ptyalism will succeed: From the collection of more dense Fluids the Bronchi will be stuffed; from a thinner matter insinuating inwardly they will be distended or their Lobes, being in some wise infected, will rise upwards; and lastly, from a settled and most gross (not to say malignant) Instuffation will arise a very dangerous Asthma." . . . "Yet, in my opinion, the Universal Taint of such Exhalations will sooner bring on that Debility in the course of an Obstinate Phthisis than if the Blood had failed in its Consistence." I leave it to the readers whether, in truth, this passage has any flavour of Harvey or not! Poor Bennet had at least the right to think out, as far as he was able, the mechanism of phthisis for he himself suffered from the disease.

¹See *Proceedings* (1914) July, 37, 517.

risk of infecting healthy brain tissue and the resulting instrumental trauma was not greater than that following the puncture in ventriculography.

Fatal cases of otitic brain abscess followed to the post-mortem room rarely showed an undrained loculus but a condition of spreading encephalitis.

Was there any evidence to show that penicillin was able to control the advance of the encephalitis?

The President said that this interesting discussion could be summed up by saying that certainly penicillin did hold out the hope of helping cases which were hopeless in the past. It had also demonstrated the need for co-operation between the otologist and the neurosurgical units, and they were very grateful to Oxford for setting such an outstanding example of this.

Professor Hugh Cairns, who replied on the Discussion, said this subject had reached a stage at which the pathology of the primary focus had become of urgent clinical interest. The use of modern antibiotics in any field of pathology raised individual problems peculiar to that field, and the question of the infection of the mastoid and petrous bone was no exception to this rule. Neurosurgeons and other people working at Oxford had been drawn closer to the otologist over the use of penicillin than they had ever been before. He thought particularly of the cases of pneumococcal meningitis where relapse occurred. The patient got cured of one attack of pneumococcal meningitis and then got another, and this sequence might go on for months, and they found themselves badgering their otological colleagues to come and tell them whether there was a primary focus in the ear which was still active and whether it ought to be operated on, rather hoping that they would say "Yes." That was just one example of the type of thing with which they were now confronted.

The dosage of intrathecal penicillin.—They were very much against large doses; the standard dosage intrathecally should be about ten thousand units in one dose. It might be given twice a day in the very acute phase of the meningitis, but for most of the time it was sufficient to give it once a day. Excessive doses could cause trouble—fits, retention of urine, and other symptoms of damage to the cauda equina. Furthermore, all the available evidence went to show that excessive dosage was unnecessary. With the dosage recommended a concentration of penicillin in the cerebrospinal fluid would be obtained which was more than ample to destroy any of the ordinary pathogenic bacteria like pneumococci or streptococci.

Intrathecal treatment must be systematic, and the least time for intrathecal treatment in a proved case of pathogenic meningitis was five days. Often it was desirable to go on for rather longer.

What penicillin could do prophylactically, both for infection at the mastoid and infection at the brain, had yet to be proved. Mr. Watkyn-Thomas put a fundamental point when he asked whether the penicillin could diffuse into the brain from the capillaries. The answer was that nobody knew, and it was an extremely difficult problem to work at experimentally. It was known that, given systemically, the penicillin would not pass in any appreciable amount into the theca. It was also known that patients who were given penicillin systemically in adequate doses would still have relapses of meningitis. Therefore, in answer to Mr. Cawthorne's question, he did not think there was any likelihood, with the present compounds, that systemic treatment would replace intrathecal treatment.

If Mr. Layton would read the opening paper he would find that they had in fact distinguished between the acute and the chronic cases. A chronic focus, where there was a collection of pus or sequestra, ought to be dealt with surgically. However, he was not clear from what had been said whether Mr. Layton would hold his hand in any case or whether he would go ahead and operate on all of them, acute and chronic, as he did in the old days. As far as osteomyelitis of the long bones was concerned surgeons had changed their views very considerably since the advent of penicillin.

Patients who got an attack of pneumococcal meningitis did not seem to become more immune, at any rate not for a long time. Relapses, of which there might be eight or nine in one case, were just as severe as the initial attack. If each attack of meningitis were treated as patiently and energetically as the first, and the surgeon in charge did not lose heart or allow the nurses to lose heart, success would be achieved and the patient would in the end cease to relapse.

There was a great field here for the otologist to work out precisely the degree to which penicillin could help him in the treatment of mastoid infection and also in its prevention in cases of otitis media.

not convinced that it is always so. "I have opened", he writes, "the Bodies of many that have died of this Disease in whom the Lungs were free from any Ulcer yet they were set about with little Swellings or stones or sandy matter throughout the whole . . . wherefore a Phthisis is better defined: 'That it is a withering away of a whole Body arising from an ill formation of the lungs'." He corrects the common error, spread among the Medical Profession, from the time of Hippocrates himself: "For what is vulgarly inferred that Phlegm falling from the Head into the Lungs and abiding there putrifies is most commonly the cause of Phthisis . . . we have previously intimated to be altogether erroneous." This upsetting of a long-established belief, on the ground, no doubt, of post-mortem examinations carefully performed, was a real service to our knowledge, made through the sagacity of Willis. Harvey's discovery appears to have had an influence upon the thoughts of this man. "This kind of Cough", he writes, "one which is catarrhal in as much as the Lympha, having passed through the Mass of the Blood, is deposited in the Lungs by the Arteries." . . . As one of the Oxford group of medical workers, he must, of course, have associated with Boyle, Hook, and others. With Lower he was an intimate friend.

Thomas Sydenham (1624-1681) we know, was a close friend of Boyle; in fact there is a letter of his to Boyle talking familiarly with the latter about the trials and occasional successes of medical practice and especially the existence of certain doctors of the baser sort! "I have the happiness", he says, "of curing my patients; at least of having it said concerning me that few miscarry under me; but I cannot brag of my correspondency with some others of my Faculty. Though yet, in taking fire at my attempts to reduce practice to a greater easiness, plainness, and in the mean time letting the Mountibank at Charing Cross pass unrailled at, they contradict themselves and would make the world believe I may prove more considerable than they would have me." Sydenham is too great and too familiar a figure to treat of in a short paper like this but there is one anecdote of his methods which I *must* quote here as an instance of his reduction of medical practice to a "greater easiness and plainness". He was called to see a gentleman who had been subjected by some other physician to a very lowering treatment and who was found by Sydenham to be "in a pitiful state of hysterical upset" occasioned, as he thought, "By the patient's long illness; partly by previous evacuation and partly by emptiness". His remedy was simple: "I therefore ordered him a roast chicken and a pint of Canary."

Sydenham's contribution to the Study of Consumption is contained in a fragment of his papers found after his death and entitled *De Phthisi*. In this short note, in which he talks of the causes of consumption and which still gives evidence, to me at least, of a definite suggestion of the influence of Harvey's work, he speaks very effectively, for that time, as to the management and of the treatment of the disease, and mentions, too, a little of the epidemiology of phthisis as it then occurred around London. "To this disease are most incident men and women from puberty to the state of life; i.e. from 15 to 25; . . . By a peculiar infelicity of our Air none are more subject to it than the inhabitants of London." He says that "the *kinds* of Phthisis differ altogether in their causes and consequently require different cures". The varieties of phthisis he describes are as follows: (1) "For a little before the Winter Solistice upon the first approach of some bitter cold, almost everyone coughs by the transpiration being suddenly checked . . . some by ill-management keep these coughs so long that the lungs are at length much debilitated by the innumerable successions that are constantly made by the act of coughing. The lungs being thus repleated with pus, from them flow purulent streams into the blood which causes a sort of putrid fever whose access is towards morning by a profuse and weakening sweat." "Lastly towards the completing of this tragedy comes on a *diarrhœa colliquitiva* . . . and then death is at hand. . . . though the Patient has all this while a serenity of mind and flatters himself with an opinion of recovery which is usual in this disease until the very last."

(2) "The second sort of consumption is laid in quite contrary season, viz. 'in the beginning of summer; for about this time a spitting of blood often happens to such young men whose blood is weak but hot and sharp, after violent exercises or a debauch of drinking'."

(3) "A third sort happens at the end of a fever, when the febrile matter is discharged upon the lungs and so, in the place of the essential fever, there succeeds a hectic . . . and, not long after, a *diarrhœa lethalis*; for they soon die of this sort of Phthisis." This division of phthisis into three does not, it seems to me, speak very well for the theoretical conceptions of Sydenham but he becomes his practical self again in his insistence upon riding as a cure for certain cases of the disease. "I am sure that if any physician had a remedy for the curing of phthisis of equal force with this of riding, he might easily get

He was pressed by medical friends to write a book on phthisis both from his own experiences and from his observations on others. His *Theatri Tabidorum Vestibulum* was the result and must have been written in or about the years 1653 and 1655. It was intended to be the introduction to a larger work but the disease, in its insistent way, called him and he was obliged to go! He died of consumption in 1655.

His book insists on the closest examination of the sputum as a guide to what is going on in the lungs. "That the Pulmonary Artery with its Divarications receives the Blood's Recrements and thence detaches them into the Branches of the Wind-pipe is a matter quite out of Dispute." He insists on the following as the varieties of sputum to be met with: "Bloody and brackish Excretions brought up by spitting at certain periods; that is, the Morning and Afternoon; more frequent Spitting and Hawking; the interception of the cutaneous and other Excretions; Globulous Spittle rolled up like Hail Stones, a dirty and ash-coloured and purulent Spittle." It is sad to remember that he must have observed all these features of the sputum in himself as well as in others. Perhaps, however, he may have enjoyed the hope which so often encourages as a part of a phthisical attack. "If by the assistance of Art the Spittle, which was variegated, be brought to one Colour; if from muddy it becomes depurated; if from an unequal Consistence it becomes smooth; if from saline, insipid; if from Stinking, without any Scent; and if, lastly, it comes Easily; it is a Sign of Recovery." He was a firm believer in the hereditary nature of the disease as often met with. Perhaps his father, John Bennet of Raynton in Somerset, may have suffered from it or his mother or some other near relative! Of this we know nothing. But he speaks of an infectious propinquity as a probable cause. "Nor are therè wanting", he says, "such as bring their constitutions with them into the World, whose Parents have died Valetudinarians or Consumptives, abounding with a cold or an immature Semen or, perhaps, over-run with an Acrimonious Heat." He goes on to quote the Hippocratic thesis at this point. "These persons"—here he refers to the offspring of the tuberculous—"have sharp shoulders which are therefore called *πτερυγίδες* (wing-like), a contracted Thorax, a narrow and low Chest, a long, thin neck, a flaccid Tone of the parts about the Breast and a very flabby Contexture of the Muscles all over the Body." It is not strange that these signs, so common in young persons exposed to contact with infection, should have been noted, as they so often were, as *causes* of consumption, but Bennet notices them as *symptoms* of the disease in those born of "valetudinarians or Consumptives" and thus is far in advance of his time.

He lays great stress on the six "Non-naturals" as he calls them which were then so much bound up with the treatment of consumptives. Richard Morton also mentioned them as well as Benjamin Marten. They are: prudence in choosing one's meat and drink; sleeping in the forepart of the night; the taking of moderate exercise; the laying aside of care, melancholy and poring thoughts; the avoidance of strong purges; and, lastly, the breathing of a pure air uncontaminated with the smoke of coals. Bennet seems to regard them as too well known to be worth putting down in detail, though Richard Morton did so, but he describes carefully how to *use* them. Why they should be called the "non-naturals" is a puzzle to me. All six seem to be natural to the last degree. But they are called "the non-naturals" both by Bennet, Morton and Marten and must have been quoted from some important and earlier work; possibly from Von Helmont or from Sylvius de la Boë! At all events great importance was attached to them in Bennet's time. His own conclusion as to exercise may be quoted: "The most proper times for Exercise are farthest from eating and drinking. . . . In the Motion and Measure of such things, both Reason and the Physician dictate that they ought to be equal to the Strength and the Times destined by Nature." He says, too, that "more brisk Exercise that opens the muscles of the Brest may sometimes be advised to those whose organs of Respiration are of a relaxed Tone and cold Temperature; as drawing the Bow, Exercise of the Pikes, etc."

Thomas Willis (1621-1675) of Christ Church in Oxford and the Sidley Professor of Natural Philosophy did not write a special book about tuberculosis but gives a valuable chapter to the subject in his *Practice of Physic*, printed by H. Clark for Dring, Harper and J. Leigh, in 1684. Born at Great Bedwin in Wiltshire, the son of a farmer who was killed, as an old man, in the Siege of Oxford, in 1646, he was evidently a loyalist and served throughout the troubles as a soldier in the University Legion. He graduated in Oxford as a B.M. and undertook practice there in 1646, the year of his father's death. He afterwards became famous as the describer of the Circle of Willis. His chapter on tuberculosis begins as follows: "Of all the Diseases of the Brest, a Phthisis or Consumption by right claims the first Place for there is none more frequent or more difficult to cure; moreover the other Affects of the Thorax being ill or not at all Cured lead into this, as lesser Streams into a Great Lake, and so ending in a Phthisis, lose both their Natures and ancient Names." He quotes the common belief that the disease is essentially an ulcer of the lungs but is

of convinced that it is always so. "I have opened", he writes, "the Bodies of many that have died of this Disease in whom the Lungs were free from any Ulcer yet they were set out with little Swellings or stones or sandy matter throughout the whole . . . wherefore a Phthisis is better defined: 'That it is a withering away of a whole Body arising from an ill formation of the lungs.'" He corrects the common error, spread among the Medical Profession from the time of Hippocrates himself; "For what is vulgarly inferred that Phlegm falling from the Head into the Lungs and abiding there putrifies is most commonly the cause of Phthisis . . . we have previously intimated to be altogether erroneous." This upsetting of a long-established belief, on the ground, no doubt, of post-mortem examinations carefully performed, was a real service to our knowledge, made through the sagacity of Willis. Harvey's discovery appears to have had an influence upon the thoughts of this man. "This kind of Cough", he writes, "one which is catarrhal in as much as the Lympha, having passed through the Mass of the Blood, is deposited in the Lungs by the Arteries." . . . As one of the Oxford group of medical workers, he must, of course, have associated with Boyle, Hook, and others. With Lower he was an intimate friend.

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what he pleased; in a word I put very many people upon this exercise in order to cure a consumption and I can truly say I have missed the cure of very few."

At a time when riding was universal and when practically nobody was unfamiliar with it, this kind of advice was probably the best by far that could be given to those cases in a fit state to get on a horse instead of sitting at home too depressed to take any kind of exercise. I can imagine that it saved many—and probably got added force from the numerous persons who suffered from chronic coughs unconnected with consumption and were, nevertheless, called phthisical.

We have already given descriptions of the works of Richard Morton and of Benjamin Marten in the *Proceedings* of the Section, but we must add a few words here.

At first a Clergyman, Richard Morton, was finally made to transfer to medicine by the Act of Uniformity which, in the words of Trevelyan, "turned adrift without compensation 2,000 of the clergy who could not record their 'unfeigned consent and assent' to everything" that the new Prayer Book contained. This was, perhaps, fortunate for the medical profession as his great book, *Phthysiologia*, is one of the only works on the subject of consumption of conspicuous merit dating from the seventeenth century. We quote his own words to describe the "Six Non-Naturals" referred to above in speaking of Christopher Bennet: "Let them also heed not to eat too much food though it be such as to afford a good Juice, as also that they do not drink too much Wine or Strong Liquors, Secondly, let them sleep in the fore part of the Night: but let them avoid sleeping in the day-time, yea, and sleeping too long in the morning; because much sleep is wont to retain and heap up a great load of Humours in the Habit of the Body. Thirdly, let them every day use moderate Exercise and Rubbing for a good while together to fetch out the dispirited Humours from the Habit of the Body by the Pores of the Skin. Fourthly, let them strictly avoid all strong Purges; for as much as they not only weaken Nature but also, by putting the Blood into too great a motion with their sharp Particles, they make it grow acrid and hot and bring it into a more serious and collicquative state; upon which a Catarrh and a Consumption are wont to follow. Fifthly, let the Patient by all lawful ways industriously lay aside Care, Melancholy and all poring of his Thoughts as much as ever he can and endeavour to be cheerful. For I have observed that a Consumption of the Lungs has had its origin from long and grievous Passions of the Mind. Sixthly, let the Patient enjoy an open, fresh and kindly air and such as is free from the Smoke of Coals, etc." Of Benjamin Marten it may be justly said that he had the wonderful imagination of a Villemain or a Koch without the facilities that came to the hands of these Masters through the strivings of Pasteur. His *New Theory of Consumptions* was one of the very best books on the subject of phthisis even apart from its almost magical adumbration of the essential cause; but it fell into complete disuse chiefly because its merits, though understandable to every medical student to-day, were then obscurely hidden from the medical profession by a whole host of dyscrasie, dispositions and other vestiges of our ancient faiths, which had to be pulled down before the rich harvest of truth could develop in its full splendour. But he had the vision! We must, I think, admit him to the position of a great Dreamer whose ideas led quietly onwards to the conception of tuberculosis in our possession at the present time.

Section of Anæsthetics

President—GEORGE EDWARDS, M.R.C.S., D.A.

[May 3, 1946]

Intravenous Pentothal as the Sole Anæsthetic for Tonsillectomy

By MAJOR CLIFFORD HAYES, R.A.M.C.

THIS report describes 82 consecutive unselected anæsthetics for the dissection of tonsils, using intravenous sodium pentothal as sole anæsthetic, without the use of any artificial air-way during operation, using the Boyle-Davies' gag only. One case had, in addition, a partial repair of a cleft palate. A large proportion of the patients were Guardsmen and of a very robust physique, with extremely difficult and adherent tonsils or remnants, one, for example, giving a history of 17 previous attacks of quinsy. Since the completion of the original series approximately another 60 cases have been anæsthetized by the same method with similar results, though no exact record of these cases was kept.

The series was originally begun merely out of interest, in fact with anticipation of failure. The surgeon, however, became so impressed with the results that he insisted on completing the series and will now use no other method of anæsthesia. Undoubtedly the main advantages are surgical but the anæsthetist's task is very much simplified, and the anæsthetic time is reduced by the length of the induction period which is shortened to a few seconds. No references are quoted in this series as it was completed overseas and the literature was not available.

Technique.—No special pre-operative preparation was used, nothing being allowed by mouth for four hours before operation. Opoidine 1/3 grain and scopolamine 1/150 grain in 1 c.c. ampoules was given by hypodermic injection at least one hour beforehand.

In the first 25 cases a 10% solution of pentothal was used with syringe and needle. In the remaining cases a 5% solution was used and given by means of a graduated vessel suspended four feet above the arm, rubber tubing, spring clip and a large bore needle (the giving needle of the Army Blood Transfusion Set). The solution was allowed to enter the vein by gravity only. The basic technique was the same for all cases, and the results and dosage appeared identical.

The operations were performed on a standard portable operating table. During induction the patient lay flat with a pillow beneath the head. The induction dose was 0.6 to 0.8 gramme of pentothal, depending on the type of patient and his response to premedication. When anæsthesia was established the pillow was removed, a sandbag inserted under the shoulders and the relaxation of the jaw tested. If this appeared satisfactory, the Boyle-Davies' gag was inserted. Otherwise, a further 1 to 4 c.c. (0.05 to 0.2 gramme) was injected first, depending on the degree of muscular rigidity persisting. In four cases, over 1 gramme was required to produce adequate relaxation of the jaw.

Maintenance dosage was based almost entirely on the depth of respiration, phonation in the smallest degree also being regarded as an indication for further pentothal. The first sign of involuntary lightening of the anæsthesia was almost always phonation, but gagging was occasionally noticed by the surgeon before phonation and was dealt with in the same way. Each additional dose was 1 to 4 c.c. (0.05 to 0.8 gramme) and, when possible, the surgeon refrained from stimulating the patient until after the resulting hyperpnœa, though this was not important except in marked lightening of the anæsthesia.

This hyperpnœa was seen in every case following repeat or maintenance doses except two in which pentothal buffered with sodium carbonate as on issue to the U.S. Army M.C. was employed. It was invariably followed by a short apnœa of 5 to 20 seconds. In 14 cases this apnœa was of longer duration due to slight over-dosage and was thus accompanied by slight cyanosis. This was quite transient and was in every case relieved by the resumption of normal respiration before any treatment could be instituted. Neither artificial respiration nor coramine was needed on any occasion.

A small stream of oxygen was run through the side tube of the Boyle-Davies' gag in the last 50 cases and this procedure was continued until the surgeon was satisfied with the hæmostasis, when the gag was replaced by a Water's metal air-way. The sandbag was then removed and a low pillow placed beneath the head. The patient was then returned to the ward and placed on his side. In none of the cases was a sucker employed and no need for one was experienced.

Total dosage has been 1.2 to 2.4 grammes, the average dose being 1.6 grammes. Operation time has been 12 to 35 minutes, the average time being 20 minutes.

A post-nasal swab was inserted as a routine by the surgeon except in the very early cases. This procedure was adopted following one case in which spasm occurred post-operatively. This was found to be due to blood which had pooled in the nose during operation and had run down into the larynx when the head was moved.

On two occasions, while awaiting complete hæmostasis, the vocal cords were examined by lifting the epiglottis, touching with a swab and thus inducing a spasm. This was completely relieved by a further dose of 0.2 gramme of pentothal.

Complications.—During the operation, when in 2 early cases a tongue plate of insufficient size was used, there was some difficulty in maintaining the air-way. In no other case was any difficulty with the air-way encountered, and indeed the ease of respiration has been greater by this method than with a large bore endotracheal catheter, since it has been so much quieter.

There is little need to stress that any foreign material entering the larynx will cause laryngeal spasm. When such a spasm was induced deliberately by direct stimulation of the larynx, it was found that both the removal of the stimulus, and the administration of further pentothal, were needed to relieve it.

On one occasion while the normal operating table was under repair, five operations were performed using a stretcher on trestles. In one patient the head became elevated, owing to the "give" in the stretcher and some coughing occurred in the early stages, until the cause was recognized and the surgeon took the necessary extra care in mopping up the blood. Then normal anaesthesia was re-established by the administration of a further 0.2 gramme of pentothal.

Post-operative respiratory spasm occurred in 6 cases and caused some degree of coughing. These all showed some cyanosis which was lessened within three minutes by the removal of the air-way. There was occasional thrombosis of the vein used for injection, and in one case a phlebitis, which lasted for five days. All these occurred following the 10% solution. These were the only post-operative complications encountered and spasm did not appear to be any worse than that seen in tonsillectomies anesthetized by other methods, and had disappeared within ten minutes.

The immediate post-operative course was remarkably improved, no patient requiring more than one dose of morphine $\frac{1}{4}$ grain and all except the 6 mentioned above sleeping quietly as in normal sleep, and eating normal meals as "up" patients in hospital "blues" on the day after operation. There was no post-operative nausea or vomiting.

Thus laryngeal stimulation and underdosage appear to be the main pitfalls as inadequate depth will cause spasm in the absence of laryngeal stimulation.

Advantages.—Induction is extremely pleasant from the point of view of the patient. The surgeon reports that he found the diminution in oozing quite striking and comparable with local anaesthesia without the concomitant œdema. The oozing was even less in those cases where oxygen was run through the side tube of the Boyle-Davies' gag.

Breathing is quiet and effortless. The minor degrees of trauma to nose and larynx occasionally inseparable from the most careful intubation are completely avoided.

The protective laryngeal reflex should persist, thus giving ample warning of the aspiration of blood by the onset of stridor. The pharyngeal reflex must be abolished this results in lax pillars with obvious advantage. Should any foreign material stimulate the larynx, control can be regained almost at once by the removal of the stimulus and the exhibition of further pentothal. With a method of anaesthesia which abolishes the laryngeal reflex this "warning-note" is absent and instant control is impossible.

The post-operative course is markedly improved especially in its early stages. (One nursing sister in the series on her first post-operative morning reported that she was far more comfortable than during her previous attack of tonsillitis.)

SUMMARY

This appears to be a safe form of anaesthesia for dissection of tonsils, offering the advantages of ease of operation for the surgeon, resulting from the effortless respiration, and complete lack of congestion. It is pleasant for the patient and offers a smooth recovery with no vomiting. The immediate post-operative period is thus much improved. It is not suggested that this method is ideal for all purposes; for the novice it is perhaps quite useless. On the other hand, it offers many advantages to the surgeon and anaesthetist provided that the latter is familiar with the minor variations in depth of anaesthesia under pentothal.

I am indebted to Major J. V. Broad, R.A.M.C., who performed all the operations in the original series for his unfailing co-operation and very many helpful suggestions; also to the Adviser in Anaesthetics, C.M.F., at that time, for much encouragement and helpful criticism, and to the Officer Commanding the hospital for his co-operation.

Personal Experience of Bronchoscopy

By GEOFFREY ORGANE, M.D.

I HAVE learnt from a personal experience of bronchoscopy many lessons which have helped me in my work.

No premedication was used that the experience might be savoured to the full and its lack seemed no disadvantage.

Anæsthetic technique.—I used amethocaine 2% in an oral spray at intervals from forty-five to fifteen minutes beforehand. It was not unpleasant and produced a definite effect on the pharynx.

This was followed by a lozenge containing 1 grain (65 mg.) amethocaine. The flavour was most unpleasant and could well be improved. The first two swallows of saliva produced retching. Salivation was profuse; this is preferable to the dryness following atropine or scopolamine—ulceration is said to have occurred where the half dry lozenge has stuck to the palate. Anæsthesia of the pharynx, tongue and lips appeared to be complete within five minutes.

In the theatre, swabs soaked in the same amethocaine solution were applied twice to each pyriform fossa. This seemed unnecessary, and the unguarded tip of the Krause's forceps on the left side produced discomfort and an attack of coughing. My tongue was held in a gauze swab—a surprisingly painful procedure, which I have since abandoned.

The intratracheal injection (through the cricothyroid membrane) of a further 2 c.c. was made in the sitting position with a fairly large needle (about size 12). There was a sensation of cold as the solution impinged on the posterior wall of the trachea, followed by uncontrollable coughing as it trickled down towards the carina. My own practice is to use a fine hypodermic needle; I feel that, with a small puncture hole, there is less chance of surgical emphysema or of cellulitis of the neck. With a larger needle the injection can be completed more rapidly and it should, therefore, be possible to withdraw it before coughing starts, so lessening the risk of breakage.

Bronchoscopy.—Passage of the bronchoscope over the dorsum of the tongue and its elevation towards the larynx produced the only discomfort of the operation, and this was only trivial. There was a sensation of stretching of the fauces which disappeared after the manipulation. There was a slight tickling feeling as it passed through the cords. As the bronchoscope approached the carina and entered each main bronchus there was uncontrollable coughing, eased in a matter of seconds by spraying local anæsthetic down the bronchoscope. The sucker was used once, producing no appreciable sensation. A gauze swab introduced into the left main bronchus caused a sense of obstruction, immediately relieved by breath-holding. The telescope down the right side increased the resistance to breathing, and down the left side produced a tickle which was relieved by breath-holding.

The presence of the bronchoscope produced no sensation whatever. Coughing through a bronchoscope feels like normal coughing.

There was no sense of pressure on the teeth. The available space between bronchoscope and teeth was appreciably increased by full hyperextension of the head on the neck. After some minutes there was aching in the temporomandibular joints.

Cerebral effects.—Cerebral stimulation was marked, with euphoria and garrulousness. Cerebral efficiency, as tested on the *Daily Telegraph* crossword puzzle, was much increased. It is not possible to attribute this to absorption of amethocaine as I afterwards discovered that, unknown to the surgeon or to myself, 100 mg. cocaine had been used in the endobronchial spray.

Post-operative course.—Anæsthesia wore off rapidly. I drank water within twenty minutes without untoward effect. At tea one hour after I could distinguish easily between the flavours of white and brown bread. There was a slight soreness in the chest during recovery, and an irritating non-productive cough. A moderate sore throat persisted for three days.

Comments.—Bronchoscopy under local anæsthesia at the hands of an expert produces only trivial discomfort—I much prefer it to a visit to the dentist!

Premedication is unnecessary and would be best confined to opiates to avoid the excessive dryness associated with atropine or scopolamine.

Local anæsthetics sprayed vigorously down the throat and nose during inspiration produce no significant anæsthesia below the vocal cords. They must be introduced directly into the trachea. The amethocaine lozenge is extremely unpleasant and its routine use before anæsthesia is an imposition on the patient. It could be improved by the introduction of flavouring materials. It is entirely effective and no further application of anæsthetic to the pharynx is needed. If the tongue is to be held forward, this should be done by the patient himself.

A post-nasal swab was inserted as a routine by the surgeon except in the very early cases. This procedure was adopted following one case in which spasm occurred post-operatively. This was found to be due to blood which had pooled in the nose during operation and had run down into the larynx when the head was moved.

On two occasions, while awaiting complete hæmostasis, the vocal cords were examined by lifting the epiglottis, touching with a swab and thus inducing a spasm. This was completely relieved by a further dose of 0.2 grammes of pentothal.

Complications.—During the operation, when in 2 early cases a tongue plate of insufficient size was used, there was some difficulty in maintaining the air-way. In no other case was any difficulty with the air-way encountered, and indeed the ease of respiration has been greater by this method than with a large bore endotracheal catheter, since it has been so much quieter.

There is little need to stress that any foreign material entering the larynx will cause laryngeal spasm. When such a spasm was induced deliberately by direct stimulation of the larynx, it was found that both the removal of the stimulus, and the administration of further pentothal, were needed to relieve it.

On one occasion while the normal operating table was under repair, five operations were performed using a stretcher on trestles. In one patient the head became elevated owing to the "give" in the stretcher and some coughing occurred in the early stages, until the cause was recognized and the surgeon took the necessary extra care in mopping up the blood. Then normal anaesthesia was re-established by the administration of a further 0.2 grammes of pentothal.

Post-operative respiratory spasm occurred in 6 cases and caused some degree of coughing. These all showed some cyanosis which was lessened within three minutes by the removal of the air-way. There was occasional thrombosis of the vein used for injection, and in one case a phlebitis, which lasted for five days. All these occurred following the 10% solution. These were the only post-operative complications encountered and spasm did not appear to be any worse than that seen in tonsillectomies anesthetized by other methods, and had disappeared within ten minutes.

The immediate post-operative course was remarkably improved, no patient requiring more than one dose of morphine $\frac{1}{4}$ grain and all except the 6 mentioned above sleeping quietly as in normal sleep, and eating normal meals as "up" patients in hospital "blues" on the day after operation. There was no post-operative nausea or vomiting.

Thus laryngeal stimulation and underdosage appear to be the main pitfalls as inadequate depth will cause spasm in the absence of laryngeal stimulation.

Advantages.—Induction is extremely pleasant from the point of view of the patient. The surgeon reports that he found the diminution in oozing quite striking and comparable with local anaesthesia without the concomitant œdema. The oozing was even less in those cases where oxygen was run through the side tube of the Boyle-Davies' gag.

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The protective laryngeal reflex should persist, thus giving ample warning of the aspiration of blood by the onset of stridor. The pharyngeal reflex must be abolished this results in lax pillars with obvious advantage. Should any foreign material stimulate the larynx, control can be regained almost at once by the removal of the stimulus and the exhibition of further pentothal. With a method of anaesthesia which abolishes the laryngeal reflex this "warning-note" is absent and instant control is impossible.

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Section of Odontology

President—LILIAN LINDSAY, M.D.S.Durham, L.D.S.Ed.

[April 8, 1946]

DISCUSSION ON DENTAL STRUCTURE AND DENTAL CARIES

Mr. E. B. Manley: I have been asked to discuss very briefly the dental structure that may be laid down within the pulp both in response to caries and also to other injuries brought about indirectly as a result of operative procedures concerned with the treatment of caries.

This is to a large extent in conformity with the broad conception of Thoma (1941) concerning dental caries. He draws attention to the fact that although it may affect clinically the calcified structures it also invokes a protective reaction that involves the entire organ. He not only regards the disease as attacking the tooth from without but he also includes the effect of the reaction that takes place from within to protect the tooth from injury and resist the invasion of bacteria.

The clinical picture of caries should include both the defence forces as well as the attacking forces. Examination of serial sections of the pulp *in situ* under carious lesions of varying degrees of severity is instructive.

It has been stated that the natural enemies of the dental pulp are bacteria and thermal changes. To these should be added two unnatural enemies, traumatic and chemical irritation, both of which may be evoked and exert their influence during the surgical treatment of dental caries. The recuperative powers of the human pulp are regarded by many as being very limited, but that this organ does in fact possess great powers of recovery can now be demonstrated with some degree of certainty. The pulp consists of undifferentiated connective tissue with a layer of highly differentiated cells, the odontoblasts. The undifferentiated connective tissue must, like all other vascular tissues of the body, have a normal mechanism of defence. This means of defence, however, is handicapped to a certain extent owing to the anatomical environment of the pulp together with the lack of a collateral circulation. In addition, however, the power to lay down calcific material in one form or another is the most potent factor of all the defence measures of the pulp. The nature of this "calcified tissue of repair" has been investigated and described in detail by E. W. Fish (1939).

The object of this communication is to illustrate from a physiological point of view some conditions under which this material can be laid down and also to refer to certain factors, other than infection, that may inhibit the process. A most severe form of injury will be used as an example, i.e. traumatic exposure of the pulp brought about during cavity preparation. Both experimental and clinical cases will be shown.

Experimental.—Premolar teeth whose removal was required for orthodontic purposes were chosen. With the use of a slowly revolving bur, cavities were cut on the gingival third of the buccal surface and a small exposure of the pulp obtained. During the cutting of the cavity the powdered fragments of dentine were carefully collected and then replaced over the exposed surface of the pulp. The cavity was then sealed with zinc-oxide clove oil paste. No other form of medication was resorted to. The teeth were extracted and serial sections prepared. One of the results is illustrated in fig. 1. After seven weeks the dentine particles have been carried into the pulp tissue and calcified material laid down around them forming a compact mass of callus in an attempt to seal off the exposed area. The particles of primary dentine and nature of the new-formed tissue is illustrated under high magnification in fig. 2 from a tooth extracted after nine weeks. The powdered dentine appears to act as an organizer and determines the differentiation of the mesenchyme cells into osteogenic cells, thus ensuring a further deposit of matrix (fig. 3). Experiments were also carried out in which the exposed surface of the pulp was touched with phenol prior to covering with zinc-oxide clove oil paste. The result is illustrated in fig. 4. A large area of pulp tissue has been completely destroyed and no new deposit of matrix can take place around the fragments of dentine which passed into the pulp at the time of exposure. The vitality of the pulp tissue was not impaired by the use of hydrogen peroxide.

Clinical (Case I, figs. 5, 6 and 7).—A traumatic exposure of the pulp horn of an upper third molar occurred during cavity preparation in January 1940. The exposed surface was covered with zinc-oxide clove oil paste without other medication of any kind. After a period of two weeks the permanent restoration was completed. The tooth was extracted in February 1945, after five years following the removal of the lower third molar. Fig. 5

Coughing during bronchoscopy may not be controllable by the patient in spite of exhortation and is rapidly relieved by further local anæsthetic sprayed down the bronchoscope. The cough sometimes found on introduction of the telescope in an otherwise quiet patient is probably due to overloading and consequent over-heating of the light bulb. In a difficult case, pressure on the teeth can be reduced by hyper-extension of the head. I have since adopted this position for direct laryngoscopy with advantage. If the patient is instructed to hold his breath before a gauze swab is introduced, one minor discomfort can be eliminated.

It is not necessary to forbid food or drink for more than one hour, at most, afterwards.

Recommendations.—There are many methods of anæsthesia available for bronchoscopy in adults, including the sledge-hammer blow of curare. Where general anæsthesia is to be used, I would advise thiopentone in sufficient dose to abolish consciousness, preceded by full local anæsthesia. The method of choice would seem to be premedication with opiates only; a lozenge containing amethocaine or nupercaine to be sucked ten minutes beforehand, or, better, a gargle of 2% amethocaine, with strict watch to see that none is swallowed; the application of local anæsthetic to the vocal cords by injection of, say, 2 c.c. 2% amethocaine through a curved laryngeal cannula passed well down over the dorsum of the tongue with the patient sitting; the introduction of 2 c.c. more into the trachea through the cricothyroid membrane or the trachea itself, or by a laryngeal cannula passed between the cords under indirect vision (direct laryngoscopy is uncomfortable); this to be supplemented by further local anæsthetic sprayed down the bronchoscope whenever indicated.

Luminous Indicators

[SHORT PRELIMINARY REPORT]

Dr. A. H. Galley said that the present use of luminous indicators on anæsthetic machines was limited to apparatus manufactured by Messrs. Coxeter and consisted of:—

- (a) A luminous plaque fixed behind Rotameter flowmeters.
- (b) Luminous handle on Coxeter-Mushin carbon dioxide absorber unit.

Dr. Galley suggested and demonstrated the following extensions of use:—

- (1) *Illumination of Flowmeters*
 - (a) Separate illuminated strip behind each flowmeter thus obviating bright luminous strips between each flowmeter and enhancing the illumination coming through each flowmeter.
- (2) *Illumination of Oxygen Controls*
 - (a) Luminous indicator hand on cylinder pressure gauge.
 - (b) Luminous control-knob for low pressure oxygen supply.
 - (c) Luminous tap (or button) for emergency oxygen flood.
- (3) *Illumination of Interior of Trilene Bottle*
Luminous semicircular plaque (with circular base) to fit on trilene bottle and illuminate interior.
- (4) *Illumination of Respiratory Movements*
 - (a) Luminous "snood" (or painted stripes) on rebreathing bag.
 - (b) Luminous brooch to pin on chest and indicate thoracic movements.

Dr. Galley said that there was a serious need for improved conditions when administering anæsthetics in complete darkness in the X-ray departments of hospitals. Although fatalities were rare there had been several instances of anoxia from the running out of oxygen supply with subsequent mental symptoms lasting in one case for over six months and retarding the development of a child. The above devices and suggestions would eliminate all possibility of anoxia; the supply of oxygen could be estimated at a glance, the controls found and manipulated without fumbling, and by means of the luminous brooch and illuminated rebreathing bag the anæsthetist could be assured of a satisfactory tidal exchange taking place. The flashing of torches was obviated, a practice which always upset the accommodation of eyesight of surgeon or radiologist.

The speaker demonstrated his apparatus and showed how fluorescent indicators could be used which would shine in different colours when subjected to light from an ultra-violet light bulb which gave off no visible rays. Various improvements in the indicators were under review, e.g. the use of a coatée embroidered with criss-cross lines of luminous plastic thread and which would replace the luminous brooch. Before final publication of these devices the British Standards Institution would be consulted with regard to standardizing the fluorescent colours used and associated with the various flowmeters (e.g. nitrous oxide could not be indicated by black luminous paint as no such entity existed—lemon yellow was used at present).

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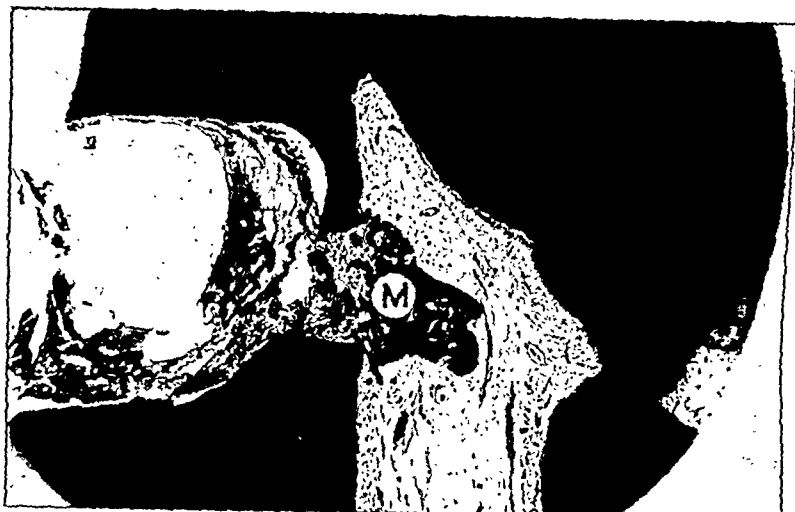


FIG. 1 ($\times 20$).—Traumatic exposure, experimental. M.: Mass of calcific material laid down around particles of dentine. After seven weeks.



FIG. 2 ($\times 283$).—P.D.: Primary dentine particles. M.: New matrix. After nine weeks.

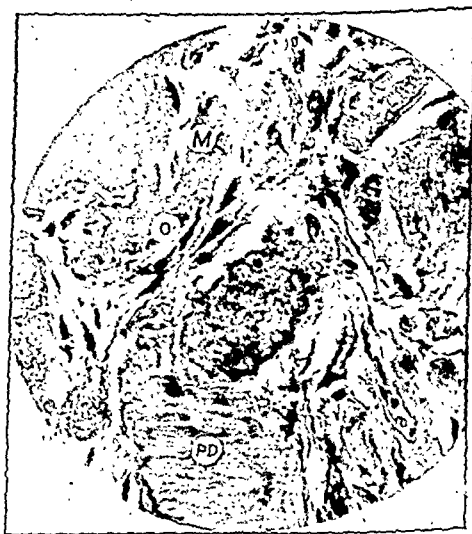


FIG. 3 ($\times \pm 303$).—O.: Osteogenic cells. P.D.: Primary dentine particles. M.: New matrix.

shows that complete recovery had taken place, the exposed area being walled off by the deposition of calcific material around some fragments of dentine which had been unavoidably pushed into the pulp tissue by the revolving bur. Fig. 6, of higher magnification, illustrates the dentine fragments embedded in the new matrix and unabsorbed after five years. Fig. 7 shows irregularly formed tubular secondary dentine at a point furthest from the site of injury and merging into the new-formed structure laid down around the dentine fragments, thus completing the seal. Other clinical cases of traumatic exposure showed that where no medication by irritant drugs had been resorted to and where there was no infection new matrix had been deposited around fragments of dentine which are invariably pushed into the pulp at the moment of exposure. A clinical case where the exposed surface had been touched with a pledget of cotton-wool moistened with phenol is illustrated in fig. 8. No clinical symptoms were manifest, the tooth being extracted after a period of fifteen months following the removal of the corresponding

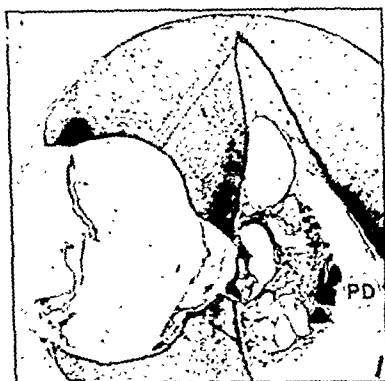


FIG. 4 ($\times 17$).—Medication with phenol. P.D.: Primary dentine fragments in damaged pulp tissue.



FIG. 5 ($\times 14$).—Traumatic exposure. Clinical. Complete recovery. Tooth extracted after five years. P.D.: Dentine fragments. M.: New matrix. S.D.: Secondary dentine.



FIG. 6 ($\times \pm 278$).—D.F.: Dentine fragments. M.: New matrix.

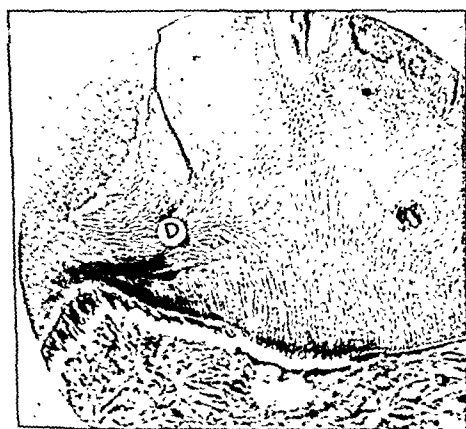


FIG. 7 ($\times \pm 233$).—D.: Tubular secondary dentine.



FIG. 8 ($\times 20$).—Clinical case. Medication with phenol. No favourable reaction. R.C.: Round-cell infiltration. A.: See text, page 24, line 3.

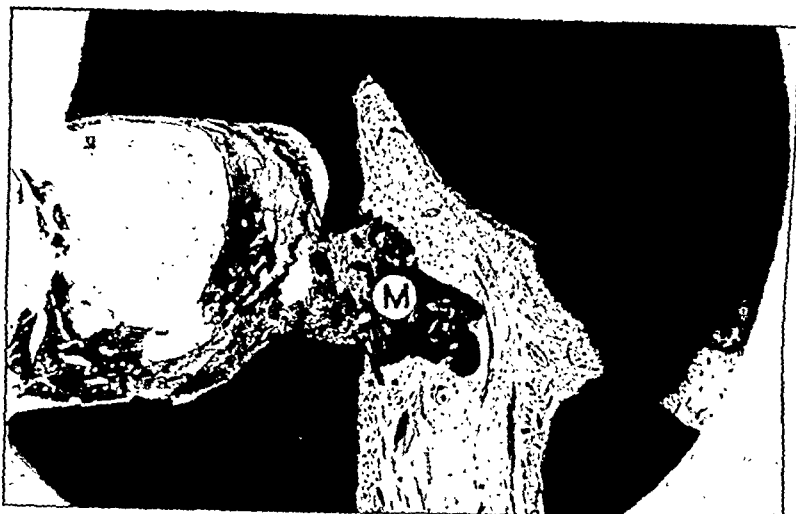


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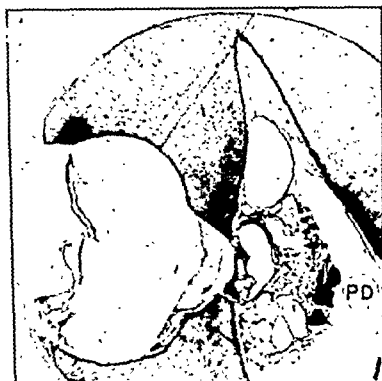


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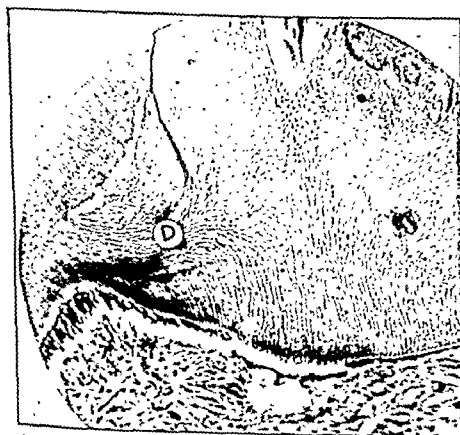


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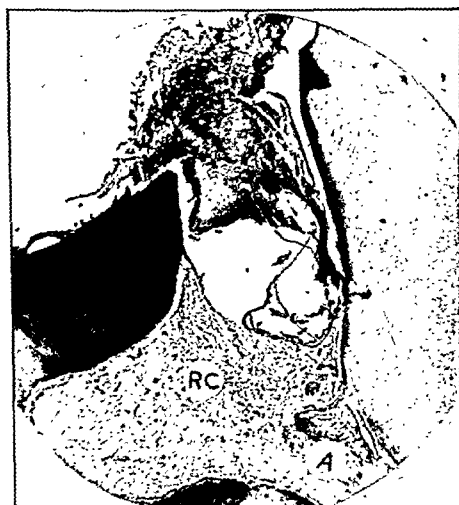


FIG. 8 ($\times 20$).—Clinical case. Medication with phenol. No favourable reaction. R.C.: Round-cell infiltration. A.: See text, page 24, line 3.

tooth in the lower jaw. Destruction of pulp tissue with a chronically inflamed area is seen. The pulp tissue has failed to react favourably and no deposition of calcific material has taken place except at the point "A" where a few fragments of dentine have reached a point outside the zone of irritation. Around them a small amount of new tissue has been laid down and become attached to the wall of the pulp chamber.

It is not surprising that no cases of repair were seen following the use of tissue-destroying drugs either experimentally or clinically. In the experimental work on pulp reaction to dental cements it was found that the ability of the pulp to form secondary dentine was impaired and sometimes completely destroyed under cavities filled with cements possessing a high degree of acidity at the time of insertion into the cavity. From a biological point of view it is essential that no irritating drugs be used.

With regard to the question of infection of the pulp: it is very necessary to distinguish between a carious and a traumatic exposure. In cases of carious exposure there will be gross bacterial infection of the pulp and no treatment other than partial or complete removal of the pulp will avail. On the other hand it is inconceivable that the pulp under the lesion described in the first clinical case should not at some period have been subject to irritation through bacterial toxins, and its recovery would lead one to believe that the pulp can tolerate a certain degree of irritation from infective sources. The question of the degree of infection that may be present under a carious lesion can only be assessed clinically at the time of the operation in each individual case.

Our understanding of the changes taking place within the pulp should aid the diagnosis of the condition requiring treatment.

Acknowledgments.—I am indebted to Mr. H. E. Heighway for the clinical material. The technical work of preparing the sections and photomicrographs has been undertaken by Mr. E. B. Brain.

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Mr. M. M. Murray: *The structure of enamel and dentine from the chemical and physical aspect.*—Although in respect of its main mineral constituents enamel is fundamentally of the same composition as the inorganic part of dentine and bone yet it is much harder. This hardness is one of the characteristic properties of dental enamel and the question presented itself as to whether, as in the case of steel, which can be hardened by the inclusion of a small proportion of other elements like tungsten, this hardness of enamel might have a similar basis. The elements suspected of causing this hardness were silicon and fluorine. Estimations of these elements in enamel were made; both were present, but the results led, at that time, to no useful deductions. In the case of fluorine, dentine often contained more than the enamel. Later work has shown that a raised fluorine content as found in the enamel of "mottled" teeth alters its properties in many ways, naked-eye appearance, permeability to stains, opacity to soft X-rays (Applebaum, 1936). It appears generally accepted that the enamel of mottled teeth is more brittle than non-mottled enamel, but according to many American investigators it is relatively more immune to caries (Dean, 1940; Armstrong and Brekhuis, 1937). The post-eruptive brown staining often seen in mottled enamel may be an expression of the increased permeability to materials in food or water; it often extends into one-third of the outer depth of the enamel.

The occurrence of organic matter in sound enamel was settled by using improved methods of enamel separation and nitrogen estimation. The amount of protein, calculated from the nitrogen, is about 2%. To what extent the acid-resistant character of enamel could be due to this protein we do not yet know, but it is significant that this protein is probably a type of keratin. Dr. Pincus has worked on the properties of this protein. Although the relative amount of organic to inorganic matter is only 2% by weight, because it has a density of 1.3 and the mineral matter a density of 3, the amount of organic matter (protein) calculated by volume is 5%.

A fairly full chemical analysis of carefully separated enamel and dentine of good, sound, permanent, premolar teeth of children gave the following results (Bowes and Murray, 1935).

TABLE I.

Percentage composition of—					Enamel	Dentine
Ash	95.38	71.09
Nitrogen	0.156	3.43
Calcium	37.07	27.79
Phosphorus	17.22	13.81
CO ₂	1.952	3.176
Fluorine	0.023	0.025
Chlorine	0.364	Nil
Magnesium	0.464	0.835
Ca/P	2.153	2.012

These figures show that the most significant difference between enamel and dentine composition is the degree of calcification or mineralization rather than the type of inorganic material laid down. Careful consideration of the figures shows, however, some differences, for example in the CO_2 and magnesium content and the Ca/P ratio. Robison (1932), pioneer worker on the biochemistry of calcification, spoke of the "bone salt" and considered that all calcification led to the deposition of one salt of constant composition and that this was a form of calcium phosphate containing combined CO_2 and called it "carbonato-apatite". This conclusion is open to criticism because there are certain differences in composition between enamel and dentine of the same tooth, for example the magnesium and carbonate content. In rodents there is a difference in composition between molar and incisor teeth.

An important point for consideration is the actual type of calcium phosphate which forms the main constituent of these structures. One clue to this is the Ca/P ratio. Calcium phosphate $\text{Ca}_3(\text{PO}_4)_2$ gives a ratio of 1.9 and the ratios for enamel and dentine preclude this and point to an apatite structure $3\text{Ca}_3(\text{PO}_4)_2 \cdot \text{CaX}_n$, which gives a ratio of 2.151. Geologists recognize several forms of apatite with X represented by either Cl, F or the OH group, giving $3\text{Ca}_3(\text{PO}_4)_2 \cdot \text{Ca}(\text{OH})_n$, which is hydroxy-apatite. Dental structures and bone are composed mainly of this substance, in which a certain amount of the calcium is replaced by magnesium. The form of combination in which the carbonate is present is still not settled. Calculations, based on certain assumptions, made from the chemical analyses gave the following composition for enamel (Bowes and Murray, 1935) (Table II)

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Fluorapatite...	0.663	0.26	0.122
Chlorapatite...	4.397	1.69	0.786
Hydroxy-apatite...	75.04	29.90	13.90
Sodium...	0.25	—	—
Loss on heating other than CO_2 and H_2O ...	1.837	—	—
Total...	97.202	37.066	16.936
Determined values (see Table I)	—	37.07	17.22

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in fluorapatite is not so great as the difference in properties might lead one to suppose. It may be pointed out here that mottled enamel and dentine contain significantly more carbonate than non-mottled. However, the value of chemical data is limited in ability to give information about actual molecular structure and arrangement and this leads to a consideration of the ultramicroscopic structure.

The interpretations of the microscopic observations on the structure of enamel present some difficulty and I am not competent to discuss this matter. I would, however, like to consider the ultramicroscopic structure as studied by X-ray—crystallographic analysis. This will summarize the work of Thewlis (1940). We collaborated in a combined chemical and physical investigation of dental enamel and various apatites (Glock, Murray and Thewlis, 1939). X-ray analysis gives information on molecular structure and arrangement and greatly extends the information obtained by chemical analysis. To illustrate this point we may compare diamond and graphite; both are composed of carbon, that is chemically identical, but whereas diamond is one of the hardest substances we know, graphite is used as a lubricant. This difference is due to a difference in arrangement of the carbon atoms in the two substances and it is from X-ray analysis that we know why they are different.

A comparison of X-ray diffraction photographs of enamel with those of some typical apatites led to the same conclusions as made from the results of chemical analyses, namely, that enamel is composed principally of hydroxy-apatite. But of greater interest is the arrangement of these apatite molecules. If molecules in any material are arranged in an orderly manner then the material is crystalline. A random arrangement is present in

tooth in the lower jaw. Destruction of pulp tissue with a chronically inflamed area is seen. The pulp tissue has failed to react favourably and no deposition of calcific material has taken place except at the point "A" where a few fragments of dentine have reached a point outside the zone of irritation. Around them a small amount of new tissue has been laid down and become attached to the wall of the pulp chamber.

It is not surprising that no cases of repair were seen following the use of tissue-destroying drugs either experimentally or clinically. In the experimental work on pulp reaction to dental cements it was found that the ability of the pulp to form secondary dentine was impaired and sometimes completely destroyed under cavities filled with cements possessing a high degree of acidity at the time of insertion into the cavity. From a biological point of view it is essential that no irritating drugs be used.

With regard to the question of infection of the pulp: it is very necessary to distinguish between a carious and a traumatic exposure. In cases of carious exposure there will be gross bacterial infection of the pulp and no treatment other than partial or complete removal of the pulp will avail. On the other hand it is inconceivable that the pulp under the lesion described in the first clinical case should not at some period have been subject to irritation through bacterial toxins, and its recovery would lead one to believe that the pulp can tolerate a certain degree of irritation from infective sources. The question of the degree of infection that may be present under a carious lesion can only be assessed clinically at the time of the operation in each individual case.

Our understanding of the changes taking place within the pulp should aid the diagnosis of the condition requiring treatment.

Acknowledgments.—I am indebted to Mr. H. E. Heighway for the clinical material. The technical work of preparing the sections and photomicrographs has been undertaken by Mr. E. B. Brain.

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Mr. M. M. Murray: *The structure of enamel and dentine from the chemical and physical aspect.*—Although in respect of its main mineral constituents enamel is fundamentally of the same composition as the inorganic part of dentine and bone yet it is much harder. This hardness is one of the characteristic properties of dental enamel and the question presented itself as to whether, as in the case of steel, which can be hardened by the inclusion of a small proportion of other elements like tungsten, this hardness of enamel might have a similar basis. The elements suspected of causing this hardness were silicon and fluorine. Estimations of these elements in enamel were made; both were present, but the results led, at that time, to no useful deductions. In the case of fluorine, dentine often contained more than the enamel. Later work has shown that a raised fluorine content as found in the enamel of "mottled" teeth alters its properties in many ways, naked-eye appearance, permeability to stains, opacity to soft X-rays (Applebaum, 1936). It appears generally accepted that the enamel of mottled teeth is more brittle than non-mottled enamel, but according to many American investigators it is relatively more immune to caries (Dean, 1940; Armstrong and Brekhuis, 1937). The post-eruptive brown staining often seen in mottled enamel may be an expression of the increased permeability to materials in food or water; it often extends into one-third of the outer depth of the enamel.

The occurrence of organic matter in sound enamel was settled by using improved methods of enamel separation and nitrogen estimation. The amount of protein, calculated from the nitrogen, is about 2%. To what extent the acid-resistant character of enamel could be due to this protein we do not yet know, but it is significant that this protein is probably a type of keratin. Dr. Pincus has worked on the properties of this protein. Although the relative amount of organic to inorganic matter is only 2% by weight, because it has a density of 1.3 and the mineral matter a density of 3, the amount of organic matter (protein) calculated by volume is 5%.

A fairly full chemical analysis of carefully separated enamel and dentine of good, sound, permanent, premolar teeth of children gave the following results (Bowes and Murray, 1935).

TABLE I.

Percentage composition of—					Enamel	Dentine
Ash	05.98	71.00
Nitrogen	0.150	3.43
Calcium	37.07	27.70
Phosphorus	17.22	13.81
CO ₂	1.952	3.170
Fluorine	0.025	0.025
Chlorine	0.364	Nil
Magnesium	0.464	0.835
Ca/F	2.153	2.012

These figures show that the most significant difference between enamel and dentine composition is the degree of calcification or mineralization rather than the type of inorganic material laid down. Careful consideration of the figures shows, however, some differences, for example in the CO_2 and magnesium content and the Ca/P ratio. Robison (1932), pioneer worker on the biochemistry of calcification, spoke of the "bone salt" and considered that all calcification led to the deposition of one salt of constant composition and that this was a form of calcium phosphate containing combined CO_2 and called it "carbonato-apatite". This conclusion is open to criticism because there are certain differences in composition between enamel and dentine of the same tooth, for example the magnesium and carbonate content. In rodents there is a difference in composition between molar and incisor teeth.

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The average size of the crystallites in human enamel is about 0.3μ in diameter. So an enamel prism which is equal to the depth of the enamel and has a breadth of 2 to 5μ must contain multitudes of these crystallites. A point of interest is that these are arranged in the prism according to some plan or pattern, that is they are preferentially orientated. Human enamel shows two plans of preferential orientation, whereas dog's enamel shows only one plan. Different areas of human enamel show different proportions of the two orientations, which will be called the 5 degrees and 40 degrees orientations, referring to the angle the crystallites make with the general direction of the fibre axis. Areas of enamel with regular prisms tend to show double orientation, in fact this predominates in human deciduous enamel. Even along an individual prism there is double orientation. The interprismatic substance also shows crystallites arranged on the plan of double orientation, but whereas the 5 degrees type predominates in the prisms, the other, the 40 degrees type, predominates in the interprismatic substance.

Enamel, both the prismatic and interprismatic substance, gives another test for crystallinity, it is birefringent. Birefringence observations confirm in all respects the X-ray findings, including the difference in crystallite arrangement between the prisms and interprismatic substance.

The study of dentine by the X-ray diffraction method is not so satisfactory, because of the greater proportion of organic matter, but the following facts can be deduced. The main inorganic constituent is again hydroxy-apatite, which exists in crystallites. These are only one-tenth of the size of those of enamel and are as a general rule arranged at random. In some cases preferential orientation was found in translucent zones of primary dentine of the root and in secondary dentine.

It is sometimes difficult to judge from ordinary microscopic study the degree of calcification of enamel in tooth sections, or to compare different areas of enamel or of dentine. For instance, is there really an outer hypercalcified layer to the enamel; are those parts of the enamel, which appear pigmented in ground section, or readily take up stain, of a different degree of calcification from the rest?

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More recently a new technique, suitable for the examination of the fine detail of hard surfaces, such as those of metals, has been employed by Gerould (1944, 1945) in the U.S.A. for the examination of tooth structure. I refer to the use of the electron microscope. This method of studying structure has advantages over the X-ray and electron diffraction methods in that a visual record on a fluorescent screen or a photographic record of the surface can be obtained.

The resolving power of the electron microscope is more than 100 times that of the best visual microscope, a magnification of 15,000 times is readily possible. Tooth sections cannot be made of the required degree of thinness, which must be less than 1μ , so surface replicas are the objects photographed. These replicas are made by covering the etched surface of the tooth, or etched surfaces of dental structure exposed in sections or by fracturing a tooth, with a plastic material, polystyrene. This makes a negative impression of the surface, which is then reproduced as a positive by depositing on the polystyrene a thin film of silica. This film, which ideally should be of the order of 0.02μ thick, is freed and floated on to a mesh grid. The actual photographs taken of this film are stereoscopic ones and so give detail in depth.

The first problem relating to dental structure investigated by this instrument was a preliminary study comparing the enamel and dentine of fluorosed and non-fluorosed teeth, which showed that the matrix of the fluorosed dentine was of much finer structure. The author (Gerould, 1945) stated that there was no difference in the interprismatic substance of the fluorosed enamel, but the photographs appear to me to show that this material has etched more readily than the non-fluorosed, which I think is possibly due to the generally greater carbonate content of fluorosed teeth.

This method is certainly very suitable for the investigation of hard surfaces and it is to be hoped that some of the electron microscopes in this country may be available for the pursuit of dental research.

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Dr. P. Pincus: Dr. Murray has mentioned the organic matter associated with enamel and I wish to bring to notice some further points concerning this organic material.

Earlier estimates of organic material are given as 2%. In 1940 Bird [1] found in 45 teeth, 4.9% organic material in enamel. As against this, Deakins and Volker [2] estimated the organic material as 0.49% to 1.95%, the highest figures being found in carious deciduous teeth and the lowest in carious, young, permanent teeth. Methods of collection and of separation are factors which may affect results. Near the dento-enamel junction, enamel tufts penetrate the enamel.

In 1943 Manly [3] found a structureless, recurrent deposit on human teeth. This adventitious material resembles a keratin and may recur within two weeks of removal. Later, Vallotton [4] divided organic coverings of enamel into two main classes, anatomical and acquired. Nasmyth's membrane, or enamel cuticle, is formed in development and remnants may persist throughout life. Acquired films are largely bacterial in composition, though Manly's film was comparatively free from micro-organisms. On examining enamel pellicle, Vallotton found some similarity to keratin in staining properties, while staining for mucin, amyloid substance and fat were negative. Limited chemical investigation of enamel pellicle failed to give Vallotton any definite indication of its nature though he confirmed Manly's report to the effect that the pellicle consists of a highly insoluble protein.

R. J. Block [5] described keratins in 1939, pointing out that the ectoderm gives rise to the enamel of teeth along with other superficial structures. He differentiates the hardening of squamous epithelium from keratinization, which is the formation of a definite horny structure. According to Block all proteins of ectodermal origin fall into two main groups: eukeratins or true keratins, and pseudo-keratins. Eukeratins resist pepsin and trypsin. Sulphur estimations on 14 keratins of different origin—hair, wool, various skins—gave the lowest sulphur determination at 2.2%, which was the value for snakeskin. When Dr. Schoeller estimated sulphur in enamel protein for me he found sulphur 1.2%.

Dr. Murray and Dr. A. Neuburger suggested testing enamel protein by two methods: (a) To compare the solubility of enamel protein with known keratins in solutions of sodium sulphide, potassium cyanide and sodium thiocacetate (b) to test the action of trypsin and pepsin on such of these proteins as then remained undissolved. The results are shown in Table I, from which it may be seen that enamel protein is a protein of a resistant nature, differing from characteristic keratins [6].

TABLE I.—RESULTS OF TESTS ON KERATINS AND ENAMEL PROTEIN.

(A) Lead acetate test		
Wool, hair, horn, hoof	All +ve	Enamel protein -ve
(B) Sodium nitroprusside test		
Wool, hair, horn, hoof	All +ve	Enamel protein -ve
(C) Solubility and enzymic hydrolysis		
(a) KCN	KCN	KCN
(b) Na ₂ S	Na ₂ S	Na ₂ S
(c) Na thiocacetate	Na thiocacetate	Na thiocacetate
Contact with one of the above for 2 days	Contact with one of the above for 4 days	Contact with one of the above for 4 days followed by trypsin for 24 hrs.
Wool	Dissolves	—
Hair	Dissolves	—
Horn	Resists	—
Hoof	Resists	Dissolves
Enamel protein	Resists	Resists

This last series of tests (C) was carried out at 37°.

(From *The Biochemical Journal* (1939) 33, 694-696.)

Enamel protein is, then, unlike hair, wool, horn and hoof, and yet it cannot be classed as one of the pseudo-keratins of Block and Vickery [7] since it is more and not less

amorphous material, such as glass. Few substances are amorphous. Crystals may be of any size, some are microscopic, some ultramicroscopic, the latter are crystallites. Enamel proved to have the molecules of apatite arranged in an orderly manner, but only over ultramicroscopic ranges, that is, enamel is composed of crystallites.

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recording that loss of calcium salts from enamel, apart from acid attack, appears possible. One may here mention Grossman [23] who estimated hydrogen-ion concentration found in carious dentine by electrometric methods; using 57 teeth, he found an average pH value of 6.51.

On the clinical side there is the work of Brucker [24] who examined over 11,000 first molars and concluded that failure of cusps to coalesce is not a factor in caries. From an examination of 6,000 children, Klein and Palmer [25] found that lower first and second molars are the teeth most susceptible to caries. Klein [26] next treated teeth of 474 children with ammoniacal silver nitrate, which he reduced with eugenol, treatment being spread over a three-month period, some teeth in each mouth being left untreated to serve as controls. Fresh attacks of caries occurred, and spread of the original carious condition extended to about the same degree in both treated and control teeth. He concluded that this treatment "does not to any significant degree prevent or arrest caries in this highly susceptible tooth".

It would therefore appear that the organic material associated with enamel is a factor in caries. This organic material is a protein of a nature resistant to enzyme and to chemical action; it also resists bacterial attack. Bacteria of course act through the enzymes they form, and such enzymes—proteinases—are often associated with a low oxygen tension such as exists in saliva [27]. Oxidation-reduction (or redox) potentials are outside the scope of this paper, as is their relation to hydrogen-ion concentration. However, addition of saliva will change methylene-blue from the oxidized (blue) state to the reduced (colourless) state. Further, material gathered from the inner surface of cheeks, lips, from between natural teeth, in fact from practically any mouth surface, will on culture give a strict obligate anaerobe, *micrococcus gazogenes*, described by Weinberg [28] as "Anaërobie strict".

From these observations it follows that a low oxygen tension exists in saliva. This condition of low oxygen tension affects determination of hydrogen-ion values as pointed out by Stephan [29]. Both Wessinger [30] and Eisenbrandt [31] attempted to correlate pH values with redox potentials; in the estimation of the latter of these, they met difficulties. Wessinger adds that deviation in pH value as estimated by quinhidrone will probably be greater the farther the redox potential is removed from zero; this lowering exists in saliva.

Further work on saliva showed in my experiments that a pyruvic dehydrogenase and an oxidase are both present in saliva, though I found it impossible to exclude bacterial growth as a possible factor in the production of these enzymes. The collection of sterile human saliva was not found possible.

Though enamel protein resists bacterial attack, attack by certain bacteria from carious material is possible. Such proteolytic bacteria may, *in vitro*, produce lesions of enamel. Lastly, saliva has been found to show reducing power, that is, conditions in the mouth may be favourable to growth of anaerobes amongst which are found bacteria capable of causing proteolysis.

Acknowledgments.—The experimental work referred to was supported by a grant from the Medical Research Council; clinical material and laboratory facilities were made available by the Royal Dental Hospital.

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- 28 WEINBERG, M., *et al.* (1937) *Les Microbes anaërobies*. Paris.
- 29 STEPHAN (1944) *J. dent. Res.*, 23, 257.
- 30 WESSINGER (1941) *J. dent. Res.*, 20, 123.
- 31 EISENBRANDT (1945) *J. dent. Res.*, 23, 247.

resistant to enzymic digestion than the true keratins. It appears to be much more resistant than human skin.

From enamel protein may I turn to matters more nearly clinical and possibly more directly concerned with caries. In 1939, following experiments by Dr. Fish [8] with dogs, I carried out experiments on sound teeth in the human mouth, teeth condemned to removal for orthodontic reasons. A cap containing methylene-blue was cemented on to the tooth. It was found that enamel stained blue in about a month and that in parts the penetration approached the dentine. It was my opinion at the time that longer exposure to the dye might have resulted in penetration to the dentine. In 1943 Berggren [9] did in fact find that methylene-blue placed in caps cemented on to human teeth in the mouth may penetrate sound enamel to the dentine. This penetration of sound enamel has been confirmed by work with radio-active substances in animals by Volker and Sognnaes [10].

From these references to enamel protein as to nature and permeability, I pass to caries. As far back as 1907 Preiswerk [11, 12] stated that caries might occur in alkaline conditions, organic ground substances being first destroyed—a disintegration brought about by proteolytic action, the calcium salts then falling out. It is possible, he stated, that caries may be produced in two ways at least (a) by acids dissolving inorganic matter and subsequent splitting-up of organic matter by proteolytic organisms, and (b) by destruction of the organic matter and as a result the setting free of the inorganic matter which then falls away.

In 1938 I attempted to separate in pure culture, bacteria which could attack enamel protein. Though pure cultures were not obtained, the cultures were narrowed down to a very small number of types. Despite this lack of success, I exposed sound teeth to cultures of known proteolytic properties and found that sound enamel was attacked in some instances [13].

(Here the speaker showed slides illustrating lesions of enamel reproduced from the *British Dental Journal*, November 1937.)

These lesions of enamel followed attack by bacteria, an attack in which acid played no part [14]. Estimations of hydrogen-ion concentration showed that the cultures remained either neutral or slightly alkaline, between pH 7 and 8. It is thought that the production of these lesions provides some evidence of the possibility of breakdown of enamel in an alkaline medium, by the attack of proteolytic bacteria. The bacteria used in these experiments were separated from carious material by routine methods.

In 1939, Gins [15] described experiments in which sound and slightly carious teeth were exposed to bacteria for periods up to fifteen months. In some cases he found further caries, which he attributed to the action of anaerobic bacteria. It was an unusual method—he placed extracted teeth in moist, sterile sea-sand, and observed, without surprise one gathers, that “normal mouth flora disappeared after three to four months”. In Gins’ opinion, saprophytic anaerobes may become pathogenic and so cause caries.

This concept of attack on enamel protein has been elaborated by Hinds [16] and by Gottlieb [17]. Hinds studied enamel in hard-ground sections and by experiments with penetration by silver nitrate. He came to the conclusion that “caries of enamel is defined as invasion of organic matter of enamel by proteolytic organisms” and that teeth differ in their resistance to penetration by silver nitrate. Gottlieb connected up proteolysis and caries, relying on microscopic examination of hard-ground and microtome preparations. Applebaum also [18] described tissue changes in enamel caries, including a translucent zone which is not decalcified.

In addition to the cases of enamel absorption previously described [14], Glickman and Bibby [19] describe a case of absorption of a buried human canine. In their photomicrographs, connective tissue is seen occupying space presumably formerly occupied by enamel, assuming enamel was present originally as it was elsewhere on the crown of this tooth.

It is obvious that absorption of dental enamel and of dentine or bone, differ inasmuch as enamel contains far less organic material.

Keeping this difference in mind, one may glance at another field of study. Brash [20] stated that “the fundamental problem of the developmental mechanics of bone is . . . the control of absorption and not of accretion of bone”. Loyatt Evans [21] quoting Brash, adds: “This general conclusion, however qualified, is inescapable. It raises reabsorption to a position of great importance and significance.” In 1943 McLean [22] pointed out “it thus appears that the decalcification of bone is a misnomer, and that the concept of the destruction of bone by resorption, involving simultaneous dissolution of both its organic and its inorganic constituents must be substituted for that of decalcification”.

By experiment I have shown that enamel *in vitro* may be lost without decalcification, and while it would be unwise to follow the comparison about bone too far, it is worth



FIG. 3.



FIG. 4.



FIG. 5.



FIG. 6.

Fig. 6 of the patient on the operating table before bandaging shows the insignificant wounds.

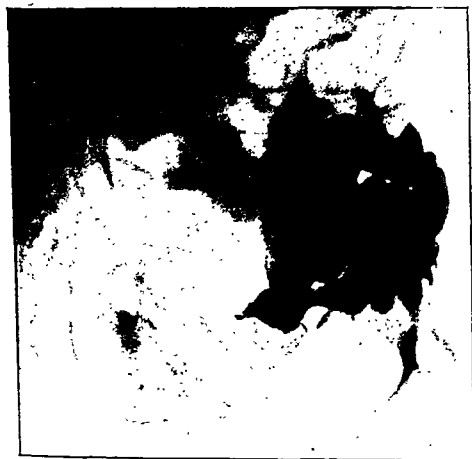


FIG. 7.

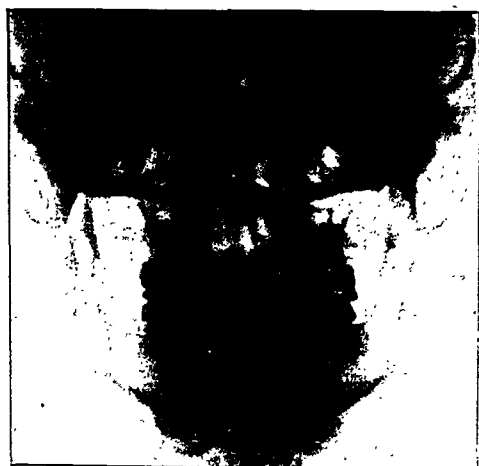


FIG. 8.

[April 29, 1946]

A Case of Kostecka's Operation for the Correction of the Prognathous Mandible

By C. BOWDLER HENRY, L.D.S.Eng., M.R.C.S., L.R.C.P.

In the whole of orthodontics there is probably no deformity so resistant to treatment, even when the child is seen early, as the elongating mandible. In this communication I am not concerned to discuss the aetiology nor the orthodontic procedures which may be tried in children to overcome it. My communication is solely to exhibit an adult patient, while still under post-operative fixation, as an example of the operation devised by Professor F. Kostecka, M.D., of Prague. Various operations have been tried, ranging from the removal of a segment of bone on each side of the mandibular corpus to sectioning the rami—Babcock, v. Eiselsberg, Limberg, Kostecka—but for simplicity, speed and lack of shock, with an adequate margin of safety from injuring important structures, no variety has appealed to me so much as Kostecka's, whose ciné-film I had seen at the Eighth International Dental Congress.

It is for these reasons that I have ventured to show the case while under treatment, instead of when finished, so the details of operation, method of splinting, pre- and post-operative radiographs may be more usefully criticized.

The patient, M. K., aged 29, was seen by Mr. H. W. Kander, L.D.S.R.C.S.Edin., Acting Dental Surgeon to the Friends' Ambulance Unit, who referred him to me on September 17, 1945, when models and photographs were taken and the operation planned. Unfortunately, owing to difficulties of in-patient accommodation, it was not possible to operate until February 25, 1946, but the delay, irritating at the time, resulted in my being able to re-establish communication with Professor Kostecka through the good offices of his former pupil—and my recent colleague—Major C. König, M.D. Prague, Chief Dental Surgeon of the Czechoslovak Armed Forces.

Professor Kostecka most generously sent me his particular mounted needle and Gigli saws and, moreover, Major König, having returned from a recent visit to Professor Kostecka's Clinic, kindly attended my operation and gave me valuable assistance and advice, which I am very pleased to acknowledge in this communication.

Pre-operative photographs, stereoscopic radiographs (Drs. Coldwell and Allchin) and dental study models were prepared. Fig. 1 shows the upper and lower models mounted on a bite-slab in the position of the patient's natural articulation. After examining these with the radiographs, I came to the conclusion that the best aesthetic result would be obtained when the chin had been translated backwards sufficiently to bring the teeth into normal occlusion. The models were therefore re-articulated empirically so as to give, as far as possible, a "normal" bite (fig. 2).

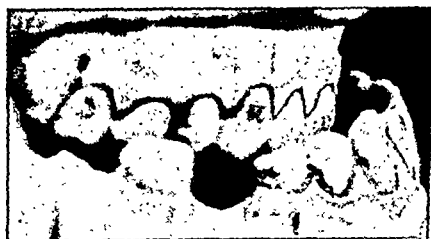


FIG. 1.

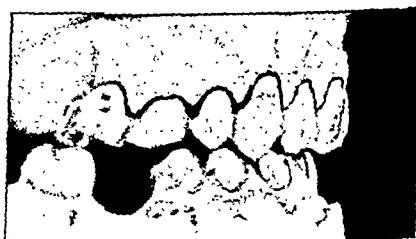


FIG. 2.

A cast metal inter-dental cap splint was then constructed for each jaw separately and a rod and tube device for locking the two members together was arranged on each side so that the splint could only be locked up when the jaw had been pushed backwards to precisely this pre-determined position of the upper and lower teeth.

On the day before operation, the upper and lower members of the splint were separated and cemented respectively on the teeth.

The operation was throughout conducted under regional novocain (2%) with omnipon and scopolamine premedication.

Both sides having been anesthetized by mandibular block and subcutaneous infiltration, Kostecka's needle was passed behind the posterior border of the left ramus and was made to emerge through the cheek close to the angle made by the anterior border of the ramus and the inferior edge of the zygomatic arch. The Gigli wire saw was attached and drawn back through the wound. With very few strokes the ramus was bisected. The right condyle was similarly sectioned (figs. 3, 4 and 5).

There was no difficulty in pushing the jaw back and immediately locking the splints in the predetermined position by passing the rods through the interdigitating tubes.



FIG. 3.



FIG. 4.



FIG. 5.



FIG. 6.

Fig. 6 of the patient on the operating table before bandaging shows the insignificant wounds.



FIG. 7.

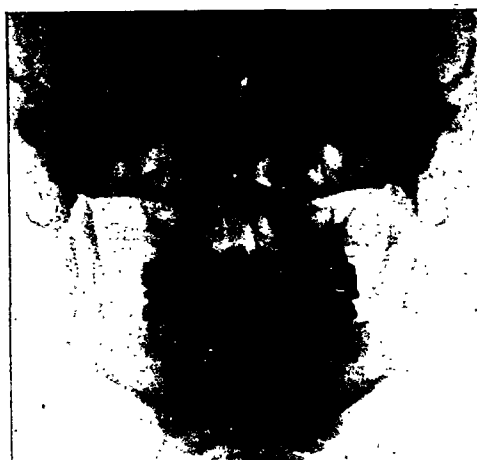


FIG. 8.

As a prophylactic I used penicillin parenterally—100,000 units daily for three days with an extra 100,000 units during operation. This was probably not necessary but I deemed it a wise precaution. Healing was uneventful.

The patient suffered some pain on swallowing for the first three days but this passed off. Trauma was minimal and neither anodynes nor re-dressings of the punctures were found to be necessary.

As will be seen from the post-operative radiographs (figs. 7 and 8), the osteotomy is made beneath the sigmoid notch and as high as possible above the mandibular foramen, thus avoiding the inferior dental vessels and nerve. In this case the operative displacement necessary to correct the profile in so gross an abnormality was, as the radiographs show, one-half of the anteroposterior width of the rami, and the anteroposterior view shows separation of the fragments on each side (fig. 8).

Figs. 9 to 11 show the case before operation and figs. 12 to 14 are photographs taken sixteen weeks after operation, at which time the mandible was functioning normally, there being neither trismus nor weakness of bite. He had been eating ordinary food for the previous eight weeks.



FIG. 9.



FIG. 10.



FIG. 11.



FIG. 12.



FIG. 13.



FIG. 14.

The further progress and the strength of the mandibular function will be watched with interest and radiographs may be shown at a later meeting.

Kostecka advocates splinting for twelve weeks. The advantages of the rod and tube device for locking the inferior member of the splint to the superior one is that, while being rigid when locked, it nevertheless allows the patient, when controlled movement is permitted, easily to withdraw the rods for meals and to reinsert them again without having to fiddle with screws.

POSTSCRIPT (30.8.46).—This patient was seen to-day. He had complete mandibular function with a strong masticatory bite and no limitation of opening.—C. B. H.

Professor R. V. Bradlaw read a communication on Oral Pathology. This was well illustrated by a large number of coloured lantern slides.

Section of Epidemiology and State Medicine

President—P. G. STOCK, C.B., C.B.E., F.R.C.P., D.P.H.

[March 22, 1946]

MEETING HELD AT THE MEDICAL SOCIETY OF LONDON, 11, CHANDOS STREET,
LONDON, W.1.

Homologous Serum Jaundice

By W. H. BRADLEY, D.M.

Senior Medical Officer, Ministry of Health

In May 1937 the two children of a well-to-do family living near Oxford died on consecutive days of acute yellow atrophy of the liver. Four days before death one child, a girl aged 7, vomited after breakfast but was able to travel with her mother to London and back by train. She vomited again after returning home, and was restless during the night. On the second day she was at first sleepy but later irritable: the restlessness became marked and she complained of some abdominal pain. Her doctor, a careful man, found no signs of physical disease and the mother chastised the child for screaming and behaving irrationally. Next day the condition changed dramatically, the child vomited altered blood, became uncontrollable and for the first time was noticed to be slightly jaundiced. She died twenty-four hours later after a period of coma with marked neurological signs.

The 4½-year-old brother's illness began a day after his sister's and ran an almost identical course. Their nurse also developed jaundice but survived.

Measles serum jaundice.—During an inquiry by Medical Officers to the Ministry of Health, it became known that, within a month, two other young children in Oxford had died of hepatic necrosis after similar illnesses and that all four and the nurse had received injections of a single batch of measles convalescent serum nine or ten weeks previously. Eventually 109 recipients of this batch of serum were traced; 41 scattered over nine widely separated areas in England subsequently became ill, 37 of them with jaundice, and 8 died of hepatic necrosis: a phenomenally high fatality rate of 12%. More significantly they all died between the 61st and 93rd day after receiving serum (MacNalty, 1937; Probert, 1938). Subsequently, and particularly as the result of inquiries made by the Medical Officer of Health for Leeds (Jervis, 1940), a few other batches of

measles serum were suspected of being icterogenic, one with fatal results, but the overall incidence amongst the thousands of persons who had received measles serum was so low that nothing was done to discourage its use. Nevertheless, the distributors of the implicated batches discontinued the preparation.

Yellow fever vaccine jaundice.—A similar sequence of events, following the administration of yellow fever vaccine, was reported by Findlay and MacCallum (1937, 1938) who, in the course of five years, had vaccinated 3,100 persons, 89 of whom developed jaundice two to seven months later. Findlay, MacCallum and Murgatroyd (1939) were satisfied that this hepatitis was not due to the yellow fever virus itself but suspected contamination with an icterogenic agent during tissue culture involving the use of human serum. They changed the strain of seed virus and observed no further cases of jaundice following the next 8,000 vaccinations (Findlay, 1940).

Jaundice with mad staggers in horses.—Both clinically and circumstantially there appeared to be a close analogy between these incidents and jaundice with mad staggers which had, on four occasions, been reported in large herds of horses during the course of immunization with various antigens administered in horse serum (Theiler, 1919; Gordon, 1935; Marsh, 1937; Stagsvold, 1938) and because of this similarity the condition was called *homologous serum jaundice*, a hepatitis characterized by a long incubation period of from two to four months following the administration of blood from the same species. Extensive investigations (1943, Medical Officers to Ministry of Health) were inconclusive but the records of these investigations were of considerable value when, in May 1942, hundreds of U.S. soldiers in transit by ship to the British Isles became jaundiced and the question arose whether they were suffering from a communicable disease and whether the convoys affected should be quarantined.

*"Post-vaccinal jaundice."*¹—It was known that during mobilization of the American Army, after the Japanese raid on Pearl Harbour on December 7, 1941, all troops received injections of yellow fever vaccine containing human serum, and in England the tentative conclusion that the men with icterus were suffering from homologous serum jaundice was reached without difficulty. Previous experience had suggested that the condition was rarely, if ever, communicable by natural routes and troop movements were allowed to proceed without restriction. These conclusions were speedily confirmed as the result of the surveys by Colonel J. E. Gordon (U.S.M.C.) in North Ireland which showed that icterogenicity was confined to certain batches of vaccine with adjacent serial numbers, strong evidence that the factor common in the implicated batches was not the tissue culture but the human serum used as a vehicle for the vaccine.

Meanwhile, in America, where the outbreak of yellow fever vaccine jaundice was first noticed in March 1942, Dr. Sawyer's team (1944) immediately began investigations amongst the U.S. troops in California, Hawaiian Islands and Oregon. The team had information concerning an earlier outbreak of yellow fever vaccine jaundice in Brazil (Fox *et al.*, 1942) where the evidence against serum used in the preparation of the vaccine was not at all convincing. However, Sawyer's studies conclusively exonerated the yellow fever virus itself for the same seed contributed to all the American vaccine while icterogenicity appeared to be associated with a few only of the lots used. In fact 9 of 117 lots investigated were responsible for 23,664 cases, an overall incidence of 56.64 per thousand doses of vaccine. On the other hand, 70 lots representing 54.4% of the entire amount of vaccine supplied to the U.S. Army during the period were associated with a jaundice attack rate of only 0.41 per 1,000 doses, a figure falling within the normal expectations of jaundice from natural causes. By chance the U.S. Navy escaped with 691 cases of jaundice associated with 1,645,740 doses of vaccine: an incidence of 1.4 per 1,000; again within normal expectation of jaundice from natural causes. The vaccine supplied to both Army and Navy came from the same source and this strange discrimination was, at first, puzzling, until it was discovered that the Navy had been supplied with a small part of one highly icterogenic batch only. With this batch 271 persons were injected and 31 developed jaundice.

This, the luck of the U.S. Navy, should be remembered for it is typical of the vagaries of incidence, resulting from accidents of distribution, which have added to the difficulties of investigating homologous serum jaundice. In consequence most of the illuminating experiences have arisen fortuitously and not as the result of organized study. One such experience played a considerable part at the time the problem of yellow fever vaccine jaundice arose in American troops approaching the British Isles.

¹ "Post vaccinal jaundice" is the term employed in American literature when referring to yellow fever vaccine jaundice.

Mumps serum jaundice.—The American Red Cross,—Harvard Field Unit at Salisbury, attempted serum prophylaxis against a mumps outbreak in a unit of the British Tank Corps stationed in Dorset. Two batches of pooled serum each from 11 volunteers recently convalescent from mumps were given to 266 and subsequently to 204 of the same men at 14-day intervals. 226 men were followed up. 44.7% developed hepatitis, 44 to 123 days later (Beeson *et al.*, 1944).

Pappataci vaccine jaundice.—A similar experience occurred in Southern Russia in 1939 but did not come to notice in England until after the events already described. In 1937 Sergiev *et al.* (1940) gave injections of active pappataci virus and convalescent serum to 500 persons in a sandfly-fever area on the Black Sea coast. These injections were innocuous. In 1939 a similar trial was made using 0.01 ml. of serum containing virus suspended in unstated quantities of serum from sandfly-fever convalescents. 92 of 350 persons who received this treatment developed jaundice within five months, the majority between the 85th and 95th day after injection. In this instance some of the pappataci virus-containing serum obtained from a patient at the onset of sandfly fever was tested by deliberate injection into four persons, one of whom developed jaundice four months later. If this single experimental case can be taken as proving that the "virus serum" was icterogenic then the main outbreak had resulted from injections of no more than 0.01 ml. of serum.

Post-transfusion hepatitis.—When these several instances (measles and mumps convalescent serum, yellow fever and pappataci vaccines) were considered together it became abundantly clear that human serum had been the vehicle of hepatotoxic agents and at the Ministry of Health it seemed inevitable that transfusions of whole blood or serum would, sooner or later, be found to result in homologous serum jaundice. However, one suggestive case only had come to the Ministry's notice: in 1941, a man with a perforated duodenal ulcer received seven bottles of whole blood and one of plasma in July at Chelmsford and developed profound cholæmia seven weeks later at Wolverhampton; but on the strength of this case a meeting of Civilian and Military Transfusion Officers and other interested persons was called at the Ministry on August 13, 1942. By a surprising coincidence the first intimation of any appreciable trouble following transfusion had been received by one of the Transfusion Officers on the preceding day. This occurred in a group of 50 patients given massive transfusions of serum and plasma by way of treatment for peripheral vascular disease. During these investigations, Morgan and Williamson (1943) traced 15 of these patients and found that 9 had become jaundiced from 49 to 107 days after the last transfusion. In five the illness was severe and protracted.

During 1943 several other observers reported cases of jaundice during the second, third and fourth months after transfusion. Some of these cases died of hepatic necrosis and in view of the comparative rarity of acute yellow atrophy of the liver, even at a time when epidemic hepatitis was prevalent, these few deaths in persons previously transfused were thought to have a significance but it was impossible to prove any direct association with the preceding transfusion. However, autopsy and biopsy material from some of these cases was compared with that from measles serum, mumps serum and yellow fever vaccine jaundice, and with N.A.B. jaundice and epidemic hepatitis, by Dible, McMichael *et al.* (1943), who concluded: "Although there may be different ætiological factors in each of the above groups, we have not found any recognizable histological criteria for their differentiation." Differentiation by other laboratory methods proved equally unhelpful and the identification, for the purposes of study, of cases of post-transfusion jaundice had to depend upon the weight of circumstances or some unusual chance such as that which brought "Batch 034" to notice (Bradley, Loutit, Maunsell (1944)). This batch of dried transfusion serum was prepared specially by the M.R.C. Transfusion Reaction Sub-Committee for the purpose of observing the immediate reactions of allergic and normal subjects to skin test doses and subsequent transfusion. Fortunately, some of the recipients remained for several weeks under observation for their allergic condition and were noticed to become jaundiced at about the same time. Follow-up showed that 57% of 75 recipients became jaundiced 45 to 104 days after injection. The incidence of jaundice was no greater in the allergic than in the normal controls. The dose had varied from 0.1 ml. intracutaneously to as much as 1,200 ml. intravenously but there appeared to be no correlation between dosage or route and virulence or icterogenicity.

The hepatitis produced by batch 034 was uniformly mild, a feature which encouraged MacCallum and Bradley (1944) to use it deliberately in the induction of jaundice in intractable cases of rheumatoid arthritis. Our intentions were benign and our objectives two in number: first, to learn something about hepatitis and, secondly, to see whether

measles serum were suspected of being icterogenic, one with fatal results, but the overall incidence amongst the thousands of persons who had received measles serum was so low that nothing was done to discourage its use. Nevertheless, the distributors of the implicated batches discontinued the preparation.

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¹ "Post vaccinal jaundice" is the term employed in American literature when referring to yellow fever vaccine jaundice.

fluid was necessarily the vehicle since some of the patients received in addition to transfusion, other parenteral therapies, for example intravenous anæsthetics or penicillin. Unless the hospital records have been grossly misleading it would appear that whole blood has been responsible for hepatitis more frequently than was at first expected. 115 histories state the nature of the blood product transfused. 24 patients received whole blood only, 20 serum or plasma only, and the remaining 71 both whole blood and a product. The experience of the Emergency Medical Service is not unique for at one time in 1945 acute massive necrosis of the liver following transfusion was the major cause of death in U.S. hospitals in the United Kingdom, accidents and pneumonia excepted.

Histology.—I was able to see the case histories and sections from 21 American soldiers dead from this cause. Coma preceded death in all cases; encephalitis was diagnosed in some and jaundice was first noticed after death in 2. The wounds for which the men were transfused were severe in half the cases only, and the patient's condition at the time of onset of hepatitis was fair or good in the majority. The histological appearances suggested that the hepatic necrosis in these fatal cases was sudden and complete and probably preceded or coincided with the onset of symptoms. The biliary passages were patent and healthy, but, unfortunately, there was no statement concerning the presence of bile in the alimentary tract. The livers of those who died before, or within a day or two, of the appearance of jaundice were virtually destroyed, yet showed minimal cellular reaction and no signs of regeneration. Phagocytic infiltration and regeneration of liver columns became more apparent as the interval between jaundice and death increased.

Treatment.—This observation, which is in line with chemical findings, has, I believe, a bearing on treatment, the rationale of which should be to support all the functions, particularly the protein function of the liver until regeneration is well advanced and to reduce energy consumption to a minimum until a weight gain is well established. Dr. Magee will comment on a hopeful line of treatment which has resulted in the only recoveries from coma I have encountered in my series of post-transfusion hepatitis.

Latent period.—Chart I, which includes under "casual" 12 deaths which have been brought to my notice, not as a result of survey, but casually by a Transfusion Officer and others, shows how characteristic is the long interval of two to four months.

Diagnosis.—When the normal expectation of hepatitis from other causes is considered in relation to the figures given for the incidence of jaundice following transfusion (see

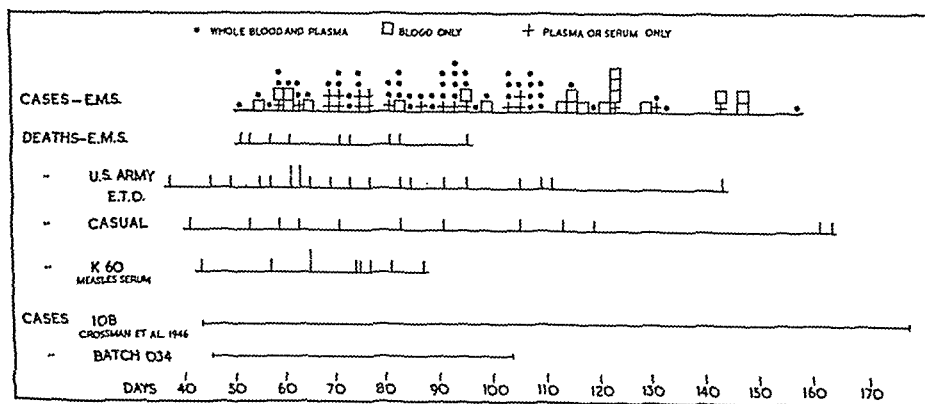


CHART I.—Duration of latent period (days) from transfusion to jaundice.

Table) the following statement appears to be justified: "When hepatitis occurs 40 to 120 days after the administration of a human blood product, or other parenteral therapy, it is almost certainly homologous serum jaundice and must be treated as a disease with an appreciable mortality."

Communicability.—MacCallum (1946) in the paper which follows this will deal with experimental transmissions, but the question still remains whether homologous serum jaundice is ever communicated naturally. I believe it is occasionally, and after a long incubation period. In a previous paper (Min. Health, 1945) an outbreak in a "gold"

Hench's (1938) claim that spontaneous jaundice gave rheumatoids a holiday from their pain was true. While I have little doubt that hepatitis, in some way, interrupts the course of rheumatoid arthritis, I feel strongly that until we understand homologous serum jaundice better it can be used as a therapeutic agent only for research purposes. However, by these experiments on rheumatoids it was proved beyond doubt that the icterogenic agent was resident in the serum and that yellow fever vaccine jaundice and batch 034 jaundice had not resulted from a natural spread of disease or from accidental syringe transmission. For by now we were beginning to suspect that outbreaks of jaundice in arspenamine, chrysotherapy and other clinics were merely examples of homologous serum jaundice, the icterogenic agent being communicated through imperfectly sterilized syringes (Min. Health, 1945).

The relative benignity of batch 034 and the regularity with which, even after two years of storage, it continued to produce jaundice in about 50% of the volunteers to which it was administered in subsequent trials, were in marked contrast to the virulence and inconsistency of another batch—045—which came under special observation. This batch was brought into use in the "allergic" trials when batch 034 was withdrawn because it had produced jaundice. It first had appeared to be innocuous until two women who had received it and other blood products intravenously died of acute yellow atrophy 97 and 105 days after transfusion. As far as could be ascertained jaundice did not occur in any other recipients of this batch of serum.

By now the Medical Research Council Transfusion Committee had begun to take part in the investigations and the transfusion officers to work out and apply measures calculated to give some control. I will not discuss these measures, which are not particularly hopeful, but will try to give you some idea of the magnitude of the problem.

The E.M.S. statistical office has searched the records of every fifth admission to E.M.S. hospitals for mention of jaundice and transfusion with the following provisional results which have been provided by Dr. Percy Stocks and Miss E. M. Brooke.

JAUNDICE INCIDENCE AFTER BLOOD TRANSFUSION.

Provisional figures obtained up to February 28, 1946, in the course of a search by the Ministry of Health's Statistical Branch at Norcross of E.M.S. Hospital records of 1940-1945 in-patients.

Group whose hospital records were examined	Total patients whose records have been examined to date	Number in whom jaundice developed during observation	Number of those who died subsequently to jaundice	Incidence rate in observation period (and standard error)
Service patients under observation 3 months or more after transfusion or injury (or who developed jaundice within that period)—				
(a) Injured patients who were transfused ...	1,316	124	17	94±8
(b) Sick patients who were transfused ...	82	16	7	(195)
(c) Injured patients who were not transfused	6,350	6	0	9±3
All males in Services aged under 35 in the United Kingdom in 1942-43	About 63,000 coded for all diseases and injuries	About 1,050 admitted with jaundice and no history of transfusion	Not ascertained	About 2 per 1,000 in 3 months

Analysis of jaundice cases in groups (a) and (c) of above table, according to theatre of war in which injury occurred.

	(a) Transfused			(b) Not transfused		
	Total examined	Jaundice developed	Died after jaundice	Total examined	Jaundice developed	Died after jaundice
Theatre of war						
Mediterranean	308	55	6	905	0	0
Western Europe	613	55	9	2,133	0	0
Far East	30	5	1	80	0	0
United Kingdom	107	8	1	1,240	3	0
Not stated	258	1	0	1,992	3	0
Total	1,316	124	17	6,350	6	0

These figures require correction because other causes may have produced jaundice. I have, therefore, scrutinized the histories of 140 cases of jaundice in transfused persons and believe that homologous serum jaundice was the most probable diagnosis in 82 per 1,000 transfused persons with a case fatality of 12%. There is, undoubtedly, a *tertium quid* somewhere in this high fatality and obviously it cannot be concluded that transfusion

fluid was necessarily the vehicle since some of the patients received in addition to transfusion, other parenteral therapies, for example intravenous anaesthetics or penicillin. Unless the hospital records have been grossly misleading it would appear that whole blood has been responsible for hepatitis more frequently than was at first expected. 115 histories state the nature of the blood product transfused. 24 patients received whole blood only, 20 serum or plasma only, and the remaining 71 both whole blood and a product. The experience of the Emergency Medical Service is not unique for at one time in 1945 acute massive necrosis of the liver following transfusion was the major cause of death in U.S. hospitals in the United Kingdom, accidents and pneumonia excepted.

Histology.—I was able to see the case histories and sections from 21 American soldiers dead from this cause. Coma preceded death in all cases; encephalitis was diagnosed in some and jaundice was first noticed after death in 2. The wounds for which the men were transfused were severe in half the cases only, and the patient's condition at the time of onset of hepatitis was fair or good in the majority. The histological appearances suggested that the hepatic necrosis in these fatal cases was sudden and complete and probably preceded or coincided with the onset of symptoms. The biliary passages were patent and healthy, but, unfortunately, there was no statement concerning the presence of bile in the alimentary tract. The livers of those who died before, or within a day or two, of the appearance of jaundice were virtually destroyed, yet showed minimal cellular reaction and no signs of regeneration. Phagocytic infiltration and regeneration of liver columns became more apparent as the interval between jaundice and death increased.

Treatment.—This observation, which is in line with chemical findings, has, I believe, a bearing on treatment, the rationale of which should be to support all the functions, particularly the protein function of the liver until regeneration is well advanced and to reduce energy consumption to a minimum until a weight gain is well established. Dr. Magee will comment on a hopeful line of treatment which has resulted in the only recoveries from coma I have encountered in my series of post-transfusion hepatitis.

Latent period.—Chart I, which includes under "casual" 12 deaths which have been brought to my notice, not as a result of survey, but casually by a Transfusion Officer and others, shows how characteristic is the long interval of two to four months.

Diagnosis.—When the normal expectation of hepatitis from other causes is considered in relation to the figures given for the incidence of jaundice following transfusion (see

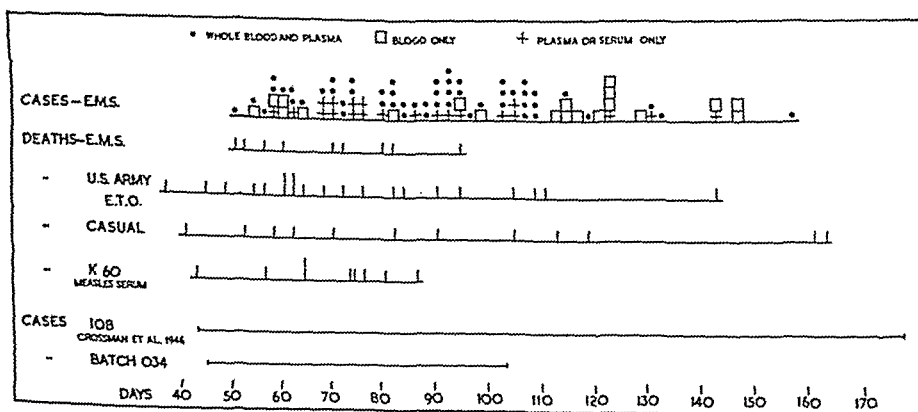
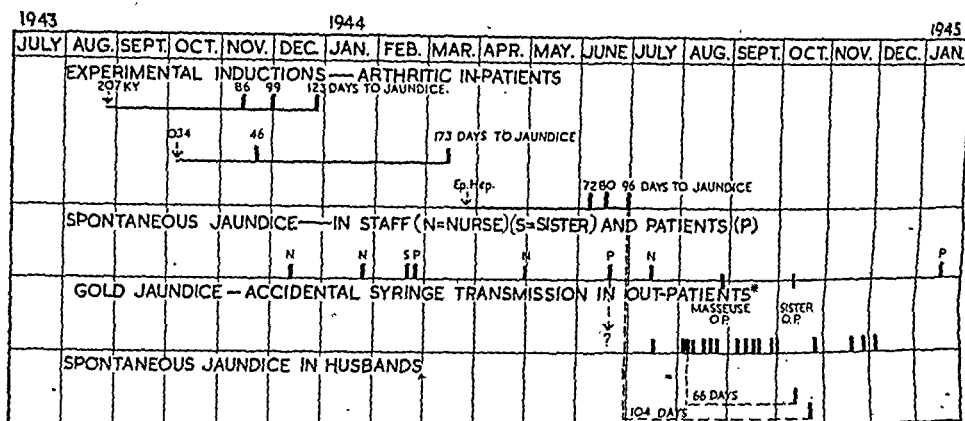


CHART I.—Duration of latent period (days) from transfusion to jaundice.

Table) the following statement appears to be justified: "When hepatitis occurs 40 to 120 days after the administration of a human blood product, or other parenteral therapy, it is almost certainly homologous serum jaundice and must be treated as a disease with an appreciable mortality."

Communicability.—MacCallum (1946) in the paper which follows this will deal with experimental transmissions, but the question still remains whether homologous serum jaundice is ever communicated naturally. I believe it is occasionally, and after a long incubation period. In a previous paper (Min. Health, 1945) an outbreak in a "gold"

clinic is described. Chart II shows the chronology of these events, and indicates the occurrence of jaundice in the husbands of two women with jaundice after intervals of 66 and 104 days.



207 KY = 2.0 c.c. subcutaneously of Batch 207 KY serum given to 10 volunteers.

034 = 50 c.c. intravenously of Batch 034 serum given to 4 patients (*vide* Bradley, Loutit and Maunsell, 1944).

EP.Hep. = 1.25 c.c. subcutaneously of serum from case of epidemic hepatitis given to 6 volunteers.

*Not more than 40 individuals at risk.

CHART II.—Dates of onset of jaundice at a rheumatism clinic.

CONCLUSION

Post-transfusion jaundice has been of considerable importance during the war. It is an unnatural hazard and doubly tragic because of this and the way in which it has so frequently brought the surgeon's efforts to naught. The need for a method of preventing it without withholding transfusion is great. Furthermore, so long as the hazard of homologous serum jaundice exists we shall hesitate to apply extensively serum or immune globulin prophylaxis in measles, mumps, epidemic hepatitis, influenza and other virus diseases which may be amenable to attenuation or prevention by this method.

Lastly, and perhaps most important, this experience with homologous serum jaundice has shown that small quantities of blood, conveyed during therapy from person to person in a variety of ways, can incidentally carry disease. Whereas jaundice is a striking clinical sign and hepatitis easily diagnosed, less spectacular infections might, on occasion, be passed round by the same means without the accidental nature of the transmission being recognized. Parenteral and blood therapies have provided us with great advantages, but we must keep a watch on them in order to detect and eliminate, as soon as possible, any undesirable features tending to vitiate or discredit them.

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Homologous Serum Hepatitis

By F. O. MACCALLUM, M.D., B.Sc.

IN 1937 MacNalty reported the first obvious cases of homologous serum hepatitis in Great Britain. The disease occurred in individuals who had been injected with pooled serum from measles convalescents or pooled serum from supposedly normal adults. At the same time Findlay and MacCallum described cases of hepatitis, probably of similar origin, in individuals who had been injected with yellow fever vaccine containing human serum. Further incidents of a similar nature occurred in Brazil, Great Britain and U.S.A. As a result of the use of blood products on a massive scale during the period 1939-1945, a sufficient number of different "outbreaks" of homologous serum hepatitis occurred to make the condition recognized as a definite entity. Because the disease could not be transmitted to laboratory animals experimental studies have been carried out in man. The information obtained by inoculation of known icterogenic sera of this type was summarized by MacCallum in 1944. Since then numerous reports of experimental work on this disease have appeared. The relevant data, old and new, which bears on the possible nature of the disease is summarized in Tables I, II and III.

TABLE I.—EXPERIMENTAL TRANSMISSION OF SERUM HEPATITIS TO MAN.

Author	Source of inoculum	Route	Dose	Recipients	Jaundice	Incubation period—days
Beeson, Chesney, McFarlan	Mumps convalescent plasma (22 donors)	I.V.	4-14.0 ml.	266	101	44-123
Bradley, Loutit, Maunsell	Dried transfusion serum—pool B	I.D. Tr.(X)	0.10 ml. 1700.0 ml.	47 17	26 10	46-104 45-96
Findlay and Martin	(1) Nasopharyngeal washings of Y.F. vaccine jaundice (2) Serum on 3rd day jaundice (3) Whole blood on 3rd day jaundice (4) Whole blood (5) Faeces on 3rd day jaundice	I.N. I.N. S.C. S.C. Oral	10.0 ml. Not given 2.0 ml. 0.5 ml. 1.0 ml.	4 5 5 2 2	3 0 0 ? 0	28,30,50 — — — —
MacCallum and Bauer	Dried transfusion serum—pool A	S.C. I.N.	0.5-2.0 ml. 2.0 ml.	11 5	4 (2) 0	59-129
MacCallum, Stewart, Bradley	Dried transfusion serum—pool B	S.C. I.N. Oral	1.0 ml. 5.0 ml. 5.0 ml.	18 10 10	9 0 0	60-114 — —
Neefe, Stokes, Rheinhold	(1) Serum (2) Faeces from serum induced cases above. 3 pools from 7 days before to 18 days after jaundice	I.V. Oral	1-100 ml. 4-15 ml.	7 19	4 0	73-100 —
Oliphant, Gilliam, Larson	(1) Y.F. vaccine (2) Pool of sera from cases in (1) (3) Pooled weekly specimens in pre-icteric stage of 1 case in (1) (4) Plasma pool 1 donor became jaundiced 4 days after bleeding	S.C. S.C. S.C. S.C. I.V.	0.5 ml. 0.5 ml. 0.5 ml. 1.0 ml. 10.0 ml.	50 10 14 15 10	12 2 4 0 0	— — 33-140 — —
Paul, Havens, Sabin, Philip	(1) Pool of sandfly fever convalescent serum (11 donors) (2) Blood from case in (1) 60 days before jaundice, 34 days after inoculation	S.C. Oral S.C.	1.0 ml. 1.0 ml. 1.0 ml.	10 3 8	4 0 3	72-94 — 74-132

S.C. = Subcutaneous

I.N. = Intranasal

I.V. = Intravenous

I.D. = Intradermal

Tr. = Transfusion

(2) = 2 Subicteric hepatitis

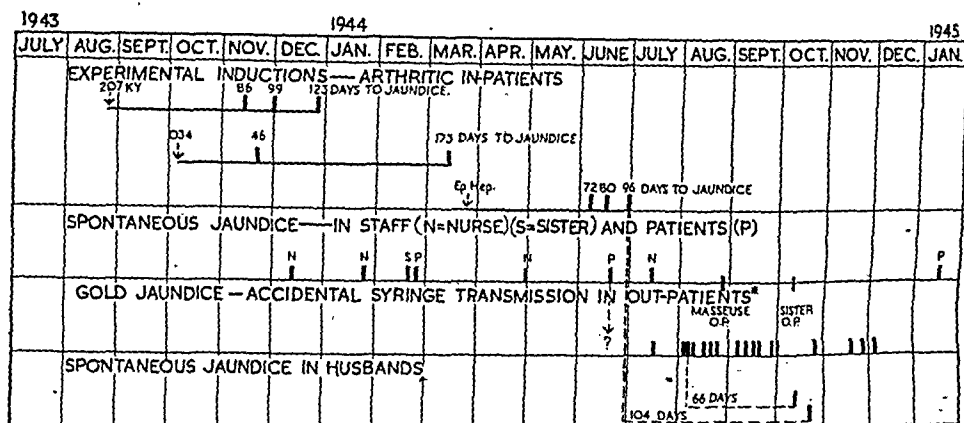
(X) = I.D. as well

TABLE II.—IMMUNITY.

Author	First attack Infective hepatitis in childhood	Reinoculation	
		Serum hepatitis No. Jaundice	Infective hepatitis No. Jaundice
Beeson, McFarlan, Chesney			
Havens	Experimental serum hepatitis		3 3
MacCallum and Bauer	Serum hepatitis Natural infective hepatitis	10 0 2 1	
Neefe, Stokes, Gellis	Experimental serum hepatitis Experimental infective hepatitis	6 0	6 2 (3) 8 0
Oliphant	Experimental serum hepatitis Experimental serum hepatitis	10 0	10 0

(3) = 3 cases of subicteric hepatitis

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SUMMARY

The available evidence suggests that the agent responsible for most cases of homologous serum hepatitis is not the same as that causing naturally occurring infective hepatitis.

The agent will pass through the usual filters which retain bacteria, but its actual size has not been determined. It is extremely resistant to heat and disinfectants, and no satisfactory method for the routine treatment of serum is known at present.

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Dr. H. E. Magee: Two Cases of Homologous Serum Jaundice.

My remarks are concerned mainly with the history of two cases of homologous serum jaundice, treated with protein hydrolysates.

Intravenous alimentation with protein hydrolysates and glucose was used in the treatment of severe cases of starvation in Holland and in the German horror camps. The treatment was not a resounding success; it was also employed with a fair amount of success in the treatment of a few cases of advanced starvation in repatriated men from Germany in the spring and summer of 1945. I have already discussed the principles of treatment in a paper given to the Section of Medicine last year (*Proc. R. Soc. Med.*, 38, 388) and again in the Milroy Lectures given in February (*Brit. med. J.*, 1946 (i) 475). After the arrival of the first case of starvation in England in 1945, the Ministry of Health established emergency supplies of hydrolysates ready for administration at Headquarters in Whitehall and in the Regional Offices throughout the country.

On September 18, 1945, Dr. ap Simon of Park Prewett Hospital telephoned me saying that he had a case which he thought might benefit from intravenous alimentation and he gave me a history of the case. At first I doubted whether it was suitable because our experience, small as it was, had been confined to cases of plain starvation, and it was for such cases that the very limited supplies of hydrolysates were intended. However, when Dr. ap Simon informed me that the prognosis was hopeless, that the patient was comatose and had not retained any food for nearly a week, I asked my colleague, Dr. Adcock, to take a sufficient supply for the case straightaway to Park Prewett Hospital. The treatment was commenced the next day.

TABLE III.—ATTEMPTS AT "INACTIVATION" OF ICTEROGENIC SERA.

I. Heat: (1) Survived 56° C. for 1 hour—routine (2) Dried Y.F. vaccine-agent survived 1½ years at room temperature									
II. Triple ether extractions in the cold MacCallum, Stewart, Bradley				Pool B		10 recipients,	10 jaundice		
III. Ultraviolet light Oliphant				(1) (a) Ictero-genic Y.F. vaccine—untreated	...	10 recipients,	2 jaundice		
				(b) Vaccine exposed for 1 hour at 2,650 Å	...	10 recipients,	0 jaundice		
				1½ hours at 2,537 Å	...				
				(2) (a) Pool of pre-icteric sera—untreated	...	13 recipients,	2 jaundice		
				(b) Serum in (a) exposed for 45 minutes at 85%, 2,537 Å	...	11 recipients,	0 jaundice		
				(3) (a) Pool of pre-icteric serum—untreated	...	9 recipients,	1 jaundice		
				(b) Serum in (a) irradiated in thin quartz cell 2½ secs. by high energy, low-pressure water, cooled mercury lamp	...	20 recipients,	0 jaundice		
MacCallum				(1) (a) Pool B—untreated	...	14 recipients,	6 jaundice		
Stewart,				(b) 30 minutes at 80%, 2,537 Å	...	10 recipients,	2 jaundice		
Bradley				(2) (a) Pool B—untreated	...	4 recipients,	3 jaundice		
				(b) 30 minutes at 95%, 2,536 Å	...	10 recipients,	1 jaundice		
IV. Phenol: Pool K 60 convalescent measles serum—still active after contact with 0.25% phenol for fourteen months									
V. Tricresol: No evidence at present									
Possible methods of control:									
(1) Gamma globulin—Addition of known immune gamma globulin to pools									
(2) Very large-pools 50,000 donors									
Small pools 10 donors									
Very small pools, or single specimens									

In 1943 Oliphant *et al.* showed that an icterogenic agent was present during the pre-icteric and early icteric stages in the blood of individuals who developed hepatitis with jaundice as a result of the injection of certain batches of yellow fever vaccine containing human serum made in the U.S.A. At the same time MacCallum and Bauer in England were able to confirm previous theories as to the origin of yellow fever vaccine jaundice by showing that an icterogenic agent was present in a pool of supposedly normal human serum collected at a blood bank and used to make certain icterogenic batches of yellow fever vaccine. Further studies of such pools have shown that they can produce hepatitis when injected intradermally, subcutaneously, intramuscularly or intravenously, but not intranasally or *per os*. Different pools of proven icterogenicity have different attack rates. The size of the inoculum has, within certain wide limits, no effect upon the attack rate, duration of the incubation period or severity of the illness. The agent has been detected circulating in the blood of one recipient thirty-four days after inoculation and 60 days before the appearance of jaundice and in another recipient seven days after the appearance of jaundice, but not two months later. A single specimen of serum collected on the seventh day of jaundice from a presumably induced case produced hepatitis and jaundice when injected intranasally, though the original pool used as inoculum did not. Transmission of the disease to man by intranasal inoculation of nasopharyngeal washings collected in the pre-icteric and early icteric stages has been reported in West Africa by Findlay and Martin. This is a contradiction of the results obtained by intranasal injection of icterogenic serum pools, but the difference may be related to the state in which the agent is present in the pools. (No successful transmissions with nasopharyngeal washings from cases of naturally occurring infective hepatitis have been recorded.) It has not been possible to transmit the disease by oral administration of faeces from cases induced by the injection of icterogenic pools. All the results of the experimental inoculation by different routes of serum and other excreta serve to distinguish the usual form of homologous serum hepatitis from naturally occurring infective hepatitis.

The reinoculation, accidentally or experimentally, of individuals convalescent from either homologous serum hepatitis or infective hepatitis suggests that homologous but not heterologous immunity is usually produced by one attack of either disease. In fact, the suggestion has been made that a previous attack of the one disease makes the individual more susceptible to the other. No explanation is forthcoming for the results of Oliphant's experiments in cross-immunity unless he had by chance selected 10 individuals who were not susceptible to infective hepatitis.

There is at present no test which will detect the presence of the icterogenic agent in a suspected serum except observation of the result of injection of the serum into man. Therefore it is desirable to obtain some method of routine treatment of all sera which will inactivate the agent, if it is present in them, without destroying the essential properties of the serum. As can be seen in Table III, the agent is extremely resistant to heat at the temperature usually used for inactivation. The effect of higher temperatures has not been tested, but most sera will coagulate when heated above 60°C. Phenol in a concentration of 0.25% has also failed to inactivate the agent.

Several experiments carried out by Oliphant suggested that the agent could be inactivated by ultraviolet light, but experiments by MacCallum *et al.* indicated that difficulties might arise in determining the suitable energy to be used and the duration of exposure. In their first experiment the supposedly suitable exposure failed to inactivate. In the second experiment the irradiation may have been effective, but when the serum was examined electrophoretically by Dr. R. A. Kekwick it was found that gross changes had occurred in the proteins. A very small residue of probably unchanged gamma globulin was detectable. Since the immune bodies in convalescent serum appear to be associated with the gamma globulin fraction this serum had been rendered useless for such a purpose. Even so, of the 10 recipients of this serum, one became jaundiced twenty-seven days after inoculation.

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The agent will pass through the usual filters which retain bacteria, but its actual size has not been determined. It is extremely resistant to heat and disinfectants, and no satisfactory method for the routine treatment of serum is known at present.

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Dr. H. E. Magee: Two Cases of Homologous Serum Jaundice.

My remarks are concerned mainly with the history of two cases of homologous serum jaundice, treated with protein hydrolysates.

Intravenous alimentation with protein hydrolysates and glucose was used in the treatment of severe cases of starvation in Holland and in the German horror camps. The treatment was not a resounding success; it was also employed with a fair amount of success in the treatment of a few cases of advanced starvation in repatriated men from Germany in the spring and summer of 1945. I have already discussed the principles of treatment in a paper given to the Section of Medicine last year (*Proc. R. Soc. Med.*, 38, 388) and again in the Milroy Lectures given in February (*Brit. med. J.*, 1946 (i) 475). After the arrival of the first case of starvation in England in 1945, the Ministry of Health established emergency supplies of hydrolysates ready for administration at Headquarters in Whitehall and in the Regional Offices throughout the country.

On September 18, 1945, Dr. ap Simon of Park Prewett Hospital telephoned me saying that he had a case which he thought might benefit from intravenous alimentation and he gave me a history of the case. At first I doubted whether it was suitable because our experience, small as it was, had been confined to cases of plain starvation, and it was for such cases that the very limited supplies of hydrolysates were intended. However, when Dr. ap Simon informed me that the prognosis was hopeless, that the patient was comatose and had not retained any food for nearly a week, I asked my colleague, Dr. Adcock, to take a sufficient supply for the case straightaway to Park Prewett Hospital. The treatment was commenced the next day.

The Park Prewett case was an Army Officer, aged 36, who on June 29, 1945, sustained simple fractures of the femur and the maxilla and a flesh wound of the leg with severe shock. He was given 1 pint each of plasma and blood. Ten days later he was transferred to Park Prewett. He then had a mild attack of bronchopneumonia but soon recovered. During this time he had been visited by a patient who became jaundiced on September 7. On September 13, seventy-six days after transfusion, evidence of hepatitis began to show and became more and more grave during the next five days. On September 18, the patient vomited dark blood and became comatose. Glucose was given by vein and rectum. On September 19, he was deeply comatose and very cyanotic. Treatment with protein hydrolysate was begun (500 c.c., equivalent to 25 g. protein, 200 calories by vein preceded by 500 c.c. of 5% or 10% glucose, 200 to 400 calories by vein). The treatment was continued until September 24, the patient receiving a total of 3,500 c.c. hydrolysate (175 g. protein, 700 calories) and 350 g. glucose (1,400 calories). The injected veins thrombosed. Improvement set in on 22nd and on 24th he was able to take food by mouth, a low fat, high protein diet. By October 4 he was practically free of symptoms. Convalescence was uneventful and he is now well.

A full report of this case was prepared by Dr. ap Simon and has since appeared in the *Lancet* (1946 (i) 492). I discussed the case subsequently with Dr. Bradley, and we arranged with Dr. Panton for the supplies of hydrolysates at Headquarters and in the Regions to be transferred to the Blood Transfusion Centres where a 24-hour service is in operation. These supplies are therefore available at call in the Transfusion Centres.

The second case was a married woman, aged 30, under the care of Dr. Williams. On November 9, 1945, an ectopic pregnancy ruptured. At operation in Llanelly Hospital she was given two pints plasma and one pint of her own blood recovered from the abdomen. On November 26 she was discharged well. On January 7, 1946, fifty-eight days after transfusion symptoms of liver damage set in and increased in severity during the next four weeks. She was readmitted to Llanelly Hospital on February 8 but deteriorated so rapidly that Dr. Williams was convinced she would die. He asked Dr. Watkin, Cardiff Blood Transfusion Centre, to see her. Her condition was very grave but she was not comatose; nausea, vomiting and continuous salivation and jaundice were marked. Dr. Watkin telephoned me on February 13, and I advised treatment with protein hydrolysate to begin at once, each dose to be preceded by 500 c.c. 5 or 10% glucose and to be given once or twice daily as he thought fit. I warned him of the likelihood of thrombosis and he gave 5,000 Toronto units of heparin before every infusion. Treatment began on February 14 when she was given by vein 400 c.c. 5-4% glucose followed by 500 c.c. hydrolysate twice. On each of 15th, 16th, 18th and 19th she was given 400 c.c. 10% glucose and 500 c.c. hydrolysate once. Improvement was apparent on 15th and by 20th she was able to take skimmed milk by mouth. Her appetite continued to improve but on 22nd it was decided to give more hydrolysate. During the infusion she had a severe rigor, vomited and then collapsed. She was given adrenaline and coramine and recovered after an hour. Improvement continued during the next three days, but soreness of the mouth, herpes and a scarlatiniform rash over the thrombosed sites of the venipunctures appeared on 25th and was general on 26th. On 27th the rash had gone and she was eating well, 1,400 to 1,600 calories a day. I saw her the next day and apart from slight jaundice and pain at the sites of injection she was quite well. Appetite and general condition improved until March 5, when she had a sudden flare-up of an old pyelitis which was practically over in forty-eight hours. By March 12 her appetite was very good and there was little jaundice. She has gone on improving and the last report I had, on March 21, said she was improving satisfactorily. During the six days of intravenous alimentation she received about 1,400 calories and the equivalent of 150 g. protein.

The Llanelly patient had many ups and downs. If only we knew the causes of the downs, it would enable us to have a better understanding of this condition and of how to treat it. Progress was not so satisfactory as in the Park Prewett case, but it should be noted that the latter received 3,500 c.c. hydrolysate in four days whereas the Llanelly case got 3,000 in six days. It may be that rapid administration from the start is the best method of treatment. I should be inclined to recommend this in any future case. The set-back in the Llanelly case on February 22 and the subsequent rash suggested a protein reaction, but the manufacturers have assured us that the hydrolysate is free from protein and from long-chain polypeptides.

Whipple (*Amer. J. med. Sci.*, 1946, 211, 149), who has done much fundamental work on protein regeneration, has shown that the 10 essential amino-acids, plus glycine, can be given by vein, or intraperitoneally for days and weeks on end to human patients, as the main or even the sole nutriment, and positive nitrogen balances and increases in body-weight have resulted. According to him, the unnatural isomers of the amino-acids are not toxic to man, but aspartic acid and especially glutamic acid are toxic when administered by vein. Casein hydrolysates like those used for these cases are relatively rich in glutamic acid. It may be that the Llanelly case was unusually sensitive to glutamic acid. Beattie (*Nature*, 1944, 153, 525) has shown that methionine alone is useful prophylactically and therapeutically in liver damage from various causes.

These digests are still in the experimental stage and more research requires to be done to bring them to the desired state of perfection. Nevertheless, there can be little doubt that the preparation used, with all its imperfections, has been mainly responsible for saving the lives of these two patients.

I have to thank Drs. ap Simon, Watkin and Williams and the Editor of the *Lancet* for their courtesy in permitting me to discuss these cases.

Professor John Beattie: The available evidence points to the conclusion that homologous serum jaundice is an infectious disease caused by an agent probably of a virus nature.

My group has been concerned with a study of the physiological and biochemical phenomena which appear during the acute and recovery phases of the disease. The disease is essentially an hepatic condition in which there are varying degrees of dysfunction and of destruction of hepatic tissue. In animals Mann has shown that signs of hepatic insufficiency do not appear until the total mass of the liver is reduced to around 20% of its normal value. If we can apply this conclusion to the disease we are studying it would appear that more than 80% of the liver may be thrown out of action—either because of disturbed function or anatomical destruction—during the acute phase of the disease. If hepatic tissue can be destroyed or rendered afunctional, to the extent suggested by Mann's experiments, before clinical and biochemical signs of hepatic insufficiency appear, it is obvious that the disease has taken hold and is progressing for some time before the critical level of insufficiency is reached.

There are some pieces of evidence which suggest that this may happen. In suspected cases of the disease admitted to hospital because of vague abdominal discomfort and slight hepatic enlargement and which later developed all the characteristic signs and symptoms, it was found on admission that a considerable loss of body-weight had already occurred varying from 2 to 10 kg., although anorexia had not developed to a degree sufficient to account for the weight loss. Nitrogen balance experiments demonstrated a marked negative nitrogen balance. The conclusion which we came to was that even before any clinical signs or symptoms—even the vaguest—had appeared, there was either an excessive destruction of body protein or alternatively that the rate of protein synthesis within the body had been reduced considerably below the normal rate of protein destruction. This state of negative nitrogen balance persisted during the acute phase of the disease and became positive with the return of appetite and other signs of clinical improvement. The positive balance was, however, due not to a reduction in the urinary nitrogen, but to an increase in nitrogen input. The rate at which the body-weight increased during the phase of positive nitrogen balance could be predicted with some degree of accuracy from the magnitude of the positive balance.

If we accept the hypothesis that homologous serum jaundice is a virus disease, we can interpret our findings along these lines. During the so-called incubation period of the disease, the virus protein is multiplying and obtaining the various specific amino-acids, which it requires to build its molecule, from the protein matrix of the body cells. If a sufficient number of liver cells are invaded by the virus, then a time will come when the liver cell cannot supply sufficient new protein for the general body needs. At that time and for some time before it the body must be in a state of negative nitrogen balance and protein requirements of the body must be met from the protein reserves in the tissues. Consequently weight must be lost. We can envisage this phase being completed without any clinical disturbance. When the virus continues to grow within the hepatic cell, a time will come when the virus will grow at the expense of the essential proteins of the cell itself and consequently necrosis takes place. The onset of clinical symptoms will date from the time when a sufficient number of liver cells are destroyed and a sufficient number rendered afunctional because of the presence of a large amount of virus body. If the process of virus growth is unchecked, the complete destruction of all the hepatic tissue takes place.

In the great majority of cases, the disease is checked, sometimes before icteric staining appears and sometimes only after a large portion of the liver tissue is destroyed. We may presume that the checking of the disease is due to the production of some specific antibody which is most likely to be of a protein nature. If this interpretation is correct, we can see that the nutritional state of the individual is a matter of some importance in determining the severity of the disease. When the protein reserves of the body are large, there will be more time for antibody to be produced before necrosis of the hepatic tissue reaches a critical level.

It must be emphasized here that this interpretation, while it does seem to fit the facts we have determined, cannot be considered as other than a tentative explanation.

We observed in severe or moderately severe cases material clinical benefit to follow the administration of large doses of methionine. In the less severe cases this benefit was not apparent to such a striking degree. We might therefore ask the question: How does methionine produce a clinical improvement? It is obvious that it cannot within a matter of a few hours or days produce a rapid regeneration of hepatic tissue. At present we incline to the view that methionine may effect clinical improvement in some part by its lipotropic action. The cells which are in process of necrosis around the intralobular virus are surrounded by a ring of cells packed with fat globules. Hence the cells are swollen and produce a mechanical obstruction to the free flow of blood to the centre of the lobule and also obstruct to some degree the bile capillaries. When methionine is given, fat is moved rapidly out of the hepatic cells and into the blood-stream. As this occurs, there is some degree of ketosis and ketone bodies appear in the urine. The final result is a rapid shrinkage of the liver and a fall in the serum bilirubin values. Nausea and vomiting, if present, disappear and there is a return of appetite.

In all probability this explanation is incomplete but it does explain why methionine is most effective when the liver is markedly enlarged and least effective when the liver is small, i.e. when necrosis is already extensive.

From the epidemiological point of view we came to the conclusion that both in this disease and in infective hepatitis, the patient was infectious for an unknown period before the onset of the first clinical symptoms. During this phase, the disease was already well established but symptoms had not appeared because (1) hepatic dysfunction and destruction had not proceeded to the stage where hepatic insufficiency developed, and (2) intrahepatic obstruction due to fat deposition had not occurred.

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or communication" with a vessel in quarantine who did not forthwith repair to an appointed lazaret, vessel or place and then perform quarantine, were liable to various pains (including pains of death), penalties, fines, forfeitures and punishments.

Whilst the passengers and crew of any vessel under quarantine could have the assistance of any medical person they desired from the shore, such medical persons, if they communicated by contact with the sick, had to perform the same quarantine as the sick persons themselves (Clause XXV).

Moreover, when it became necessary for the Medical Attendant on the staff of the Superintendent of Quarantine to inspect the sick, he was required to keep his boat to windward of the vessel in which the sick were at a distance of not less than ten feet and if any patient, after being examined in this manner, was found to require special medical or surgical aid he was removed to a hospital ship. Apparently the last of these old hulks was the hospital ship "Fleming," which lingered on in Plymouth Sound until 1930.) The Quarantine Acts were not finally repealed until 1896 but long before then they had been regarded as a failure. As far back as 1849 the subject had been discussed by the General Board of Health for England and Wales (at that time the Central Health Authority for the country) and it was even then contended that quarantine could give but a false sense of security.

The General Board of Health was replaced in 1858 by the Privy Council as the Central Health Authority for England and Wales and in 1865 Sir John Simon, the Medical Officer of the Privy Council, in an official memorandum [1] on the subject of quarantine summed up heavily against such useless restrictions and paper plausibilities.

"A quarantine which is ineffective is a mere irrational derangement of commerce; and a quarantine of this kind which ensures success is more easily imagined than realized. Only in proportion as a community lives apart from the great highways and emporia of commerce, or is ready and able to treat its commerce as a subordinate political interest, only in such proportion can quarantine be made effectual for protecting it. In proportion as these circumstances are reversed, it becomes impossible to reduce to practice the paper plausibilities of quarantine. The conditions which have to be fulfilled are conditions of national seclusion."

In 1871 the Privy Council issued several Orders, under which Customs officers were empowered to visit and examine ships and to detain those infected or suspected to be infected with cholera. The ship had to be moored where the Customs officers directed and no person could land whilst the ship was so detained. The Customs had then to notify forthwith the local sanitary authority, who were empowered to visit and examine the vessel before it could enter port. Infected persons had to be removed to hospital and bedding and clothing disinfected or destroyed, the measure taken depending on the results of medical inspection without any undue detention of the ship.

Later in the year (1871) the Privy Council were succeeded by the Local Government Board as the Central Health Authority, and the passing of the Public Health Act, 1872, gave the Board power to constitute for the first time Port Sanitary Authorities either by designating one or by uniting two or more of the sanitary authorities (referred to as Riparian Authorities) whose district or part of whose district forms part of or abuts upon any part of a port or the waters of such port. Their jurisdiction was over all the waters within the limits of the port and also the whole or such portion of any Riparian Authorities as might be specified, and the Local Government Board had powers to assign to Port Sanitary Authorities any powers, rights, duties, capacities, liabilities and obligations under the Sanitary Acts.

The expenses incurred by a Port Sanitary Authority were defrayed out of a common fund contributed to by the Riparian Authorities included in the Port Sanitary Authority in such proportions as the Local Government Board thought just, a subject which will again be referred to.

In a way a dual system of control then arose for although the Quarantine Act, which was administered by the Privy Council, was rapidly falling into disuse quarantine was still practised to a limited extent for yellow fever. But this was not primarily on medical grounds but solely with the view of relieving our Maritime commerce from disabilities which would otherwise have been imposed upon it by other countries in which quarantine was regarded as an essential part of their health administration.

The last occasion when a vessel arrived with yellow fever actually on board was in 1865 [2]. On September 9 of that year the sailing barque "Hecla" reached Swansea from Cuba with three men suffering from yellow fever. Deaths had occurred during the voyage, but the disease was not declared when the vessel arrived. The weather at the time was exceptional and the heat is described as being almost tropical. Between September 15 (i.e. six days after her arrival) and October

¹No exhaustive search has been possible but from the records consulted the only Quarantine Station or Hospital on an island in the United Kingdom was on the Flat Holm Island in the Bristol Channel (about three miles to the southwest of the entrance to the Cardiff Docks). It is not clear when the station was first established but the arrangements are referred to in the Annual Report of the M.O.H. of Cardiff for 1889. A crematorium was added in 1893 but landings could only be effected in fine weather and the Hospital was finally closed in 1933.

[May 24, 1946]

Progress and Problems in Port Health Administration

By P. G. STOCK, C.B., C.B.E., M.B., F.R.C.P., Hon.F.R.C.S.Ed., D.P.H.

(President of the Section of Epidemiology and State Medicine)

INTRODUCTION.—About one hundred years ago—to be exact, on September 15, 1849—a letter appeared in the *Lancet* signed "Pater", urging the formation of a society to study epidemic disease. The ravages of cholera had recently carried off some 50,000 to 60,000 of the population of these Islands and "there was abroad an earnest desire to render another visitation of this disease, if not preventable, less disastrous in its results". The Epidemiological Society of London was founded in the following year (1850) becoming in 1907, on the amalgamation of various medical societies, the Epidemiological Section of the Royal Society of Medicine and in 1913 the Section of Epidemiology and State Medicine.

Amongst the many distinguished Presidents who preceded me was Dr. Richard Reece, who occupied the Chair in 1922/23 but died from influenza and overwork the following year. Reece was then Senior Medical Officer in the newly-formed Ministry of Health and chose as the subject for his Presidential Address "Progress and Problems in Epidemiology" (*Proc. R. Soc. Med.*, 1923, 16, Section Epidemiology, p. 35). I am convinced, however, that since his early days in the Port of London, before he joined the staff of the old Local Government Board, Reece's greatest interest lay with the welfare of those who "go down to the sea in ships", and consequently to everything that pertained to port health administration.

As it was under Reece's guidance that I had the honour to join this Section when I was a newly-appointed member of his staff, and had no conception that in the course of time I should succeed either to the post he held at the Ministry or to this Presidential Chair, I trust you will bear with me in paying this brief tribute to one of your former Presidents and for choosing as the subject for my Presidential Address to-day "Progress and Problems in Port Health Administration".

I. MARITIME TRAFFIC

The last Quarantine Act in this country was passed in 1825 and, whilst consolidating and modifying the Acts previously in force, it still enjoined detention and strict isolation

Under Clause II of the Act the places appointed for the performance of quarantine were Standgate Creek; Whitebooth Roads, between Hull and Grimsby; Bromborough Pool or Milford Haven; Motherbank near Portsmouth; St. Just's Pool within the mouth of the Harbour of Falmouth; King Road and Portshute Pill; Inverkeithing Bay (Firth of Forth); and Holy Loch in the Firth of Clyde. A number of places were similarly appointed for vessels bound to Ports in Ireland.



for specified periods of persons coming from ports considered to be infected, regardless of whether actual cases had occurred; and if cases occurred on the ship during the quarantine period an indefinite prolongation of the quarantine resulted. Various places were appointed for vessels to perform quarantine and any persons having "any intercourse

or communication" with a vessel in quarantine who did not forthwith repair to an appointed lazaret, vessel or place¹ and then perform quarantine, were liable to various pains (including pains of death), penalties, fines, forfeitures and punishments.

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In a way a dual system of control then arose for although the Quarantine Act, which was administered by the Privy Council, was rapidly falling into disuse quarantine was still practised to a limited extent for yellow fever. But this was not primarily on medical grounds but solely with the view of relieving our Maritime commerce from disabilities which would otherwise have been imposed upon it by other countries in which quarantine was regarded as an essential part of their health administration.

The last occasion when a vessel arrived with yellow fever actually on board was in 1865 [2]. On September 9 of that year the sailing barque "Hecla" reached Swansea from Cuba with three men suffering from yellow fever. Deaths had occurred during the voyage, but the disease was not declared when the vessel arrived. The weather at the time was exceptional and the heat is described as being almost tropical. Between September 15 (i.e. six days after her arrival) and October

¹No exhaustive search has been possible but from the records consulted the only Quarantine Station or Hospita on an island in the United Kingdom was on the Flat Holm Island in the Bristol Channel (about three miles to the south-west of the entrance to the Cardiff Docks). It is not clear when the station was first established but the arrangements are referred to in the Annual Report of the M.O.H. of Cardiff for 1889. A crematorium was added in 1893 but landings could only be effected in fine weather and the Hospital was finally closed in 1933.

13, 22 cases occurred in Swansea in which the diagnosis of yellow fever seemed fairly certain, and 7 other cases in which the circumstances of exposure and the character of the attack led to a more or less strong suspicion that the illness was of the same nature. Of the cases diagnosed as yellow fever, 15 died and 7 recovered. Of the doubtful cases, 1 died and 6 recovered.¹

After the creation of Port Sanitary Authorities the system² depended essentially on medical inspection and the detention of a vessel only so long as was necessary to inspect those on board, to deal with the sick and carry out any necessary measures of disinfection.

The machinery set up under the Quarantine Acts for obtaining information as to health conditions on vessels from foreign was made use of for dealing with all diseases on incoming ships, and the "quarantine" questions which Customs officers were required to put to the Masters of vessels from foreign were continued as part of the routine in port sanitary districts, and Customs officers continued to visit, examine and detain ships. Under the Public Health Act, 1875 (Sections 130 and 134), powers were given to the Local Government Board to make regulations in regard to cholera and such other diseases, both on land and on the high seas, within three miles of the coast.

The first survey of the port and riparian sanitary districts by medical inspectors of the Local Government Board was carried out in 1886 and in consequence of the rapid diffusion of cholera throughout Russia in the summer of 1892 an emergency survey of the chief English ports was instituted. There were then 60 Port Sanitary Authorities in England and Wales and some 60 or 70 Riparian Authorities where there was shipping, but the old river ports of Tudor times such as Cambridge, Norwich, Oxford and York had lost their importance. In consequence of the unsatisfactory character of the then current arrangements in many of the districts visited, and in view of the continued prevalence of cholera in Europe a more detailed and deliberate survey of the whole coastline was started early in 1893 and completed in 1894.

Only a general summary of the findings can be attempted here but the Report [3] on the survey which was published in 1895 is full of interest. In his introduction Sir Richard Thorne, the Medical Officer³ to the Local Government Board, stated that when the survey was started (in 1892) it was found that in only one-third out of a total of 60 Port Sanitary Districts could the general administration be regarded as satisfactory and efficient but by the time the more detailed survey was completed the majority of the port and riparian districts were fairly well organized, so far as action under the cholera orders was concerned.

"For the purposes of cholera some means of hospital isolation was from the first found in 44 out of the 60 ports, and in 9 others it was provided after the inspector's visit. Ambulance boats were available in a number of the more important ports; provision existed in the great majority of the ports for the destruction by burning, or the disinfection, of clothing, &c.; and, with but few exceptions, some arrangements had been made as to the emptying of water-tanks on board ship, the provision of a proper water supply, and the pumping of bilges. The arrangements for the medical inspection of vessels and of persons, under the Board's Orders, were found to be satisfactory in all but five port districts. He added that in certain of them, notably, the ports of London, the River Tyne, Hull and Goole, Southampton, Weymouth, Plymouth, Bristol, Cardiff, Barry-and-Cadoxton, Swansea, and Liverpool, the arrangements were not only highly satisfactory in themselves, but they were carried out with a devotion to duty on the part of many of the Medical Officers of Health, such as must be regarded as having largely contributed to the marked success with which imported cholera was controlled at nearly all English ports during 1892 and 1893."

Demands were made at the time to revive Quarantine against infected ports but were firmly refused, and Sir Richard Thorne pointed out that:

"Port or Riparian Sanitary Authorities have imposed upon them the duty of so dealing with ships, either infected with cholera or arriving from places infected with cholera, that the sick shall be placed in hospital; that those suspected of cholera shall be detained for a limited period so that the nature of their illness may be ascertained; that certain sanitary measures such as efficient disinfection of vessels shall be carried out; and that prior to the landing of healthy persons their addresses at the places of destination to which they are travelling shall be obtained. Should cholera succeed in passing this outer line of defence, trust is placed for the prevention of its spread, in the general sanitary administration of the country."

As already stated, the quarantine enactments were finally abolished by the Public Health Act of 1896, which gave the Local Government Board power to enforce any Regulations made by them under the Public Health Act of 1875, with the assistance of the officers of Customs and Coastguards, as well as other Authorities. The Public Health (Ports) Act of 1896 enabled the Board to assign to Port Sanitary Authorities, powers

¹ See also the case of the "Sea Rambler" which arrived in the River Tyne in September 1936 from West Africa.

Ann. Rep. C.M.O., Min. of Health, 1936, p. 195.

² It was not, however, until the International Sanitary Conference of Vienna in 1874 that such a system rather than the old form of quarantine was accepted by a majority of the delegates.

³ The designation "Chief Medical Officer" was first used when the Ministry of Health replaced the Local Government Board in 1919.

under the Infectious Diseases (Prevention) Act and a series of General Regulations dealing with Cholera, Yellow Fever and Plague were issued by the Board. The passing of the Infectious Disease (Notification) Extension Act of 1899 made the notification of the more serious infectious diseases compulsory in every urban, rural and port sanitary district in England and Wales.

Another landmark was the formation of the Association of Port Sanitary Authorities¹ in 1898, when, during a conference of the Royal Sanitary Institution in Birmingham, representatives of the Port or Riparian Sanitary Authorities of Cardiff, Dover, Hull and Goole, Manchester, Newport, the River Tyne and Yarmouth met and started the Association.

The spread of plague to Europe in 1899 led to the International Sanitary Convention in 1903 and to implement this Convention, the Local Government Board issued, in 1907, a fresh series of Regulations (which had chiefly to be carried out by Port Sanitary Authorities) in regard to cholera, yellow fever, and plague on ships arriving from foreign countries; and as to cholera and plague on outward bound and coasting ships in the event of this country becoming infected by one or other of these diseases.

These Regulations took cognizance of the part played by rats in the spread of plague which had then been established, and in 1909 the Board started the issue of a "Weekly Record" of reported occurrences of plague, cholera and yellow fever (in ports at home and abroad) for the information of Port Medical Officers of Health. At first it was only neostyled and was a very incomplete affair, but the scope was gradually extended and in 1919 was printed and an extended distribution made.

The Regulations of 1907 were the last published by the Local Government Board as, owing to the War of 1914-18, an amended series drawn up to implement the International Sanitary Convention of 1912 was never issued.

At the end of the war the whole question of Port Health Administration was carefully reviewed and it was considered desirable to take special steps for guarding against the introduction of disease in view of the prevalence on the Continent of smallpox, typhus, relapsing fever and the increased risks to which this country was exposed by the amount of movement which the close of the war and demobilization were likely to produce.

It was recognized that the extended services which Port Sanitary Authorities would be required to provide were for the benefit of the country generally and not merely of the particular locality in which the ports were situated and a decision was reached—perhaps long overdue—that expenditure on efficient Port Sanitary Administration should be partially met by the Exchequer.

Regulations under which the Ministry of Health (which had then replaced the Local Government Board) would pay grants were issued in 1920 and authorized 50% of the approved expenditure in respect of the whole work of Port Sanitary Administration. This was defined as including expenditure on medical and other staff, provision and maintenance of isolation hospitals, disinfection and disinfection stations, the provision of facilities for chemical and bacteriological investigations, transport for the boarding of vessels, the administration of the Foreign Meat and Unsound Food Regulations, the work undertaken by Port Sanitary Authorities in the execution of the Public Health (Shellfish) Regulations, 1915, or otherwise in the supervision of shell fisheries and any other services required or approved by the Ministry.

At the same time, the Minister issued the Port Sanitary Authorities (Infectious Diseases) Regulations, 1920, which placed new responsibilities on these Authorities and their Medical Officers of Health in addition to those already imposed by the Cholera, Yellow Fever and Plague Regulations of 1907, which continued to apply to these diseases.

In certain circumstances, when the presence of infectious disease on a ship was suspected, a more extended medical examination of persons entering the country was required than had been undertaken hitherto. The Medical Officer of Health was empowered to board any ship for the purpose of the Regulations and to cause the ship to be brought to, and, if necessary, moored or anchored in, some safe and convenient place while it was visited and examined. In deciding whether he should use his powers to board a particular ship and examine persons on board, the Medical Officer of Health had to a large extent to exercise his discretion but in the covering circular to the Regulation the Minister expressed the view that the fact that a vessel during the period of *three* weeks before its arrival in port, had sailed from, or called during the voyage at, a foreign port or country in which dangerous infectious disease is known to be prevalent, would constitute reasonable ground for such action being taken.

Incidentally the covering circular pointed out that: "The more common infectious

¹ Now the Association of Port Health Authorities of the British Isles.

diseases such as scarlet fever and measles did not, in the Minister's opinion, save in exceptional instances, call for special action."

The Regulations authorized measures to be taken against other infectious diseases, notably typhus and smallpox, which in some respects were comparable to those required under the old Regulations (1907) for cholera, yellow fever and plague.

On the issue of the 1920 regulations, an extended survey of the Port and Riparian Sanitary Districts was carried out by a team of medical officers of the Ministry working under Dr. Reece, the inspections being followed in due course by conferences with each of the Sanitary Authorities concerned when the new Regulations and matters requiring attention were discussed.

These inspections also afforded opportunities for discussion with Port Medical Officers of Health of questions connected with the medical inspection of aliens for which they had become responsible at the Ports approved, by the Secretary of State, for the landing of aliens. (The cost of this service falls on the Exchequer.)

There were then 60 Port Sanitary Authorities and some 40 Riparian Authorities in England and Wales at which there was shipping, but in 1922, the Riparian Authorities of Dover and Folkestone were made Port Sanitary Authorities with jurisdiction over certain land areas in the immediate vicinity of the harbours.

During these inspections special attention was paid to the position of the mooring stations required under the Cholera, Yellow Fever and Plague Regulations of 1907 and the information then collected eventually led to the modifications introduced by the Port Sanitary Regulations of 1933. In the past sentimental consideration had frequently resulted in the selection of remote and often inconvenient places for mooring stations and one in the Bristol Channel was so unfortunately sited that a vessel proceeding there, before the days of wireless, might, in foggy weather, neither be seen from nor able to signal to the shore.

It may well be claimed that the issue of the new Regulations and the 50% grant, which enabled them to be carried out, together with the series of visits and conferences raised the whole standard of Port Health Administration and gave many Port Medical Officers of Health the opportunity to attain the state of efficiency they desired.

Probably the most important matter dealt with in the 1920 Regulations was the prevention of the danger of the spread of infectious diseases by vermin, especially by the deratization of ships. Towards the close of the (1914-18) war the possibility of plague being introduced into this country by infected rats occasioned anxiety. The subject is dealt with at length in a paper by Reece, which is printed in the Chief Medical Officer's Report for 1919-20, and appended to the paper are tables showing the number of vessels that arrived at Ports in England and Wales from 1895 to 1920 on which plague or suspected plague among men and rodents had occurred on the voyage. Time and space do not permit of the tables being brought up to date in this paper but the short reference seems pertinent as the facts set out were one of the factors which led up to the 1920 Regulations. Sea-borne commerce had been disorganized by war conditions and such anxiety as existed was not lessened by the increasing "ratty" condition of ships. Much of the merchandise which had accumulated at certain ports abroad afforded excellent opportunities for the harbourage of rats as well as ample food and facilities for nesting and breeding. Owing to the shortage of vessels and the necessity for avoiding all delays, ships had to be turned round as quickly as possible and the six-monthly deratization of ships which had been recommended in the International Sanitary Convention of 1912 and which, prior to the war (1914-18), was becoming usual throughout the world, fell into abeyance and there were many indications that the rat population of the Mercantile Marine had vastly increased. To give an extreme example after the fumigation of the S.S. "Khiva," with sulphur candles, in the Royal Albert Docks on January 6, 1920, nearly 1,500 rats were found dead and 35 loads of refuse were removed from the holds. Other countries were faced with the same problem for which some authorities considered complete fumigation of the ship was the only panacea.

The United States incorporated in their 1920 Quarantine Regulations a definite requirement that all vessels engaged in trade with foreign ports should be fumigated simultaneously in all parts either with sulphur dioxide gas or hydrogen cyanide. Early in 1922 these requirements were more strictly enforced and the American Public Health Authorities insisted that even the first and second class passenger accommodation of our large transatlantic liners should be included. Shipowners were then faced with the alternatives of complying with these Regulations or having their vessels quarantined on arrival in American ports—with the consequent enormous loss on "demurrage". To fumigate the passenger accommodation with sulphur dioxide gas, with the consequent damage to fittings and the loss of time required to make good, was held on economic

grounds, to be out of the question, the practical alternative being the use of hydrogen cyanide, a method employed by U.S. Quarantine Authorities since 1913.

The first vessel to be deratized with sulphur dioxide¹, at an English Port (the River Tyne) was the S.S. "Royal Dane" on December 22, 1899, but hydrogen cyanide had not been employed until Cunard Liner "Scythia" (19,730 tons gross register) was fumigated throughout at Liverpool on March 17, 1922. The long story of the fumigation of ships is outside the scope of this address and only occasional references can be made, but to give some idea of the extent to which fumigation was then being practised in America, the following figures are of interest. In the Port of New York during the twelve months ending June 30, 1922, 1,425 vessels with a total tonnage of 4,671,292 tons and an average tonnage of 3,418 were fumigated. The total rats recovered after fumigations was 6,925 or an average of only 4.8 rats per vessel.



Dr. Richard Reece and Surgeon-General H. Cumming, Quarantine Station, Craney Island, U.S.A., August 1922.

As it was considered desirable that inquiries on the whole question should be made in America, Dr. Reece and myself were sent to the United States in August 1922 to confer with the Surgeon-General of the Public Health Service, Dr. Hugh Cumming, and his staff, and to investigate their methods of fumigation. As a result of this visit, arrangements were made whereby certificates of Fumigation issued by certain Port Sanitary Authorities, approved by the Minister of Health, would be accepted by the Quarantine Authorities of the United States. The Port Medical Officers of Health of Bristol, Cardiff, Hull and Goole, Liverpool, London, Manchester, Southampton and Swansea (and subsequently Newport, Barry, Falmouth and Sunderland) were authorized to issue the special certificates (Form Port 10) and in November 1922 instructions were issued by the Minister in regard to the fumigation of vessels to comply with the requirements of the U.S.A.

That the part rats play in the spread of plague was fully realized in this country is illustrated by the following extract from a Circular (No. 374) which was issued by the Ministry of Health in January 1923 with the object of drawing the attention of County Councils to the need for delegating, to Port and Riparian Authorities, their jurisdiction under the Rats and Mice Destruction Act of 1919. This Act applies to vessels and gives Port Sanitary Authorities additional powers for dealing with vessels infested with rats, though experience has shown that the application of the Act to a particular vessel is sometimes difficult. In urging such delegation, the Ministry pointed out:

"Among the more important functions of Port and Riparian Sanitary Authorities under the Public Health Acts is the prevention of the introduction and spread in this country of ship-borne plague. For this purpose it is desirable that, in addition to their powers under the Public Health Acts, they should be able to take measures under the Rats and Mice (Destruction) Act, 1919, for the destruction of rats both on board ship and also on the quays, wharves and warehouses abutting upon the port."

Section 103 of the Quarantine Regulations of the United States (1920), which deals with the routine fumigation of vessels, was revised in January 1923, so as to allow for the extension of the period of six months in the case of vessels complying with the following conditions:

- (1) Vessel constructed so as not to favour or encourage the harbourage of rats.
- (2) Vessel plying regularly between ports not infected with plague.
- (3) Vessel regularly carrying no cargo, or cargo of such nature, or so packed or stowed, that it cannot serve as rat food or rat refuge.
- (4) Vessel has been regularly certified as loading in stream from rat-free lighters, or as complying with the regulations relative to fending off from docks, proper use of guards on lines and hawsers, raising or guarding of gangways and ladders, and docking at rat-free docks or wharves.

¹Liquid sulphur dioxide in cylinders was used.

The possibilities of rat-proofing continued to receive attention in the United States and the publication of an article on the rat-proofing of vessels in the Public Health Reports for July 17, 1925, aroused such widespread interest, especially among shipbuilders and shipowners, that the article was translated subsequently into several languages. A second and larger edition was published in December 1926.

Writing in his Annual Report for 1927, Sir George Newman stated:

"Though rat-proofing on shore is now a recognized practice the same cannot be said in regard to the application of the principles of rat-proofing in ships. Yet this is a matter which merits the serious consideration of naval architects, shipbuilders and shipowners. There can be little doubt that when the new International Sanitary Convention comes into operation the rat-proof ships will be at a great advantage over others when the question of the issue of a deratization exemption certificate has to be decided. It is frequently difficult and expensive, and it may be impossible, to make existing buildings or ships fully rat-proof, though many improvements can be effected in this direction by practical attention to minor details. In new construction, however, whether of buildings or ships, the application of the principles of rat-proofing should be neither difficult nor expensive and will fully repay any additional cost incurred."

A few Port Medical Officers of Health took the greatest interest in rat-proofing—notably Dr. Maurice Williams of Southampton—and a certain amount of rat-proofing was done on British vessels such as those of the Cunard S.S. Company—but it is the tramp rather than the mail steamer that carries plague. A third edition [†] of the American Memorandum was published in 1931 which covered all phases of rat-proofing as applied to ships both new and old, and copies were sent to the Medical Officers of Health of the Ports approved for the issue of Deratization and Deratization Exemption certificates. A further Report on Rat-proofing of new ships was published in 1939.

The benefits claimed in the U.S.A. from rat-proofing are summarized in a paper published in their Public Health reports for December 24, 1943, and when visiting the Quarantine Station, New York, in August 1943, it was learnt that it had never been necessary to fumigate a single vessel for the destruction of rats which had been constructed and structurally maintained in accordance with the rat-proofing specifications of the United States Public Health Service.

In June 1944 the Ministry of War Transport issued a memorandum on the rat-proofing of new ships and there seems little doubt that more and more attention will be paid to this method of combating the menace of rat plague.

Whilst Port Health Authorities in this country probably now regard rat-plague and smallpox as public enemies No. 1, they have many other responsibilities and the International Agreement of Brussels¹, for securing the gratuitous treatment at seaports of seamen when suffering from venereal disease, which was ratified by this country in 1925, added another to the list.

The next great advance resulted from the International Sanitary Convention of 1926 which was signed by the representatives of 66 countries and subsequently ratified by 44. It provides for the *immediate* notification by Governments to other Governments and to the Office International d'Hygiène publique of cases of plague (*including rodent plague*), cholera, yellow fever, epidemic typhus and smallpox, the last two diseases now being included in an International Sanitary Convention for the first time. When the formal conference was held in Paris to consider the draft revisions which had been prepared by the Office International, delegates still had in mind the disastrous pandemic of influenza in 1918-19 but a proposal to include influenza among the diseases dealt with in the Convention was not accepted, though subsequently the severe outbreak of dengue which occurred in Greece and other Mediterranean Countries in 1928 led to the International Convention for Mutual Protection against Dengue Fever of 1934.

The Convention, however, settled the much-disputed question of the procedure to be followed for dealing with the rat population in ships and preventing the spread of plague. Briefly, all vessels of signatory countries, except those engaged in national coast-wise trade, must be inspected at regular intervals of six months, to ascertain whether there are on board more than a minimum of rats. Any vessel on which there is evidence that the rat population is in excess must be subjected to deratization and a "Certificate of Deratization" on an approved form must be issued by the competent Authority. If, on the other hand, there is little or no evidence of rats in any vessel at the time of inspection a "Certificate of Exemption from Deratization" likewise on an approved form, must be granted. These Certificates will be recognized in the ports of other countries which have ratified the Convention and, in the absence of the occurrence of special circumstances such as plague amongst the rats on board, will exempt vessels from further fumigation during the six months following the issue of the Certificate.

¹ This agreement, which was initiated by the British Delegate, Sir George Buchanan, in May 1920 was drawn up by the Permanent Committee of the Office International d'Hygiène publique and after circulation to Governments by the Belgian Government, was signed at Brussels on December 1, 1924.

To implement these requirements the Permanent Committee of the Office International d'Hygiène publique drew up an international form of certificate. This was adopted and issued—as form Port II—with an explanatory memorandum to the Port Medical Officers whom the Minister of Health had authorized to grant such certificates. To provide more fully for the application of the relative article (No. 28) of the new Convention the Public Health (Deratization of Ships) Regulations were issued in October 1929. And, to ensure a reasonable degree of uniformity at the designated ports in England and Wales provisional standards for the fumigation of ships for the destruction of rats were issued. At that time 16 ports had been approved (and duly notified to the Office International) for the issue of Certificates and the naval ports of Chatham-Sheerness, Devonport and Portsmouth were also designated, at the request of the Admiralty, for the issue of Certificates to naval vessels.

During 1927-30 an unusual number of vessels arrived with rat-plague or suspected rat-plague on board. As an instance the case of the S.S. "Plutarch" may be quoted, which has an additional interest as this was the first occasion on which a loaded ship was fumigated in this country with HCN. The "Plutarch" arrived in the Port of London in June 1927 with a cargo of grain from the River Plate and during the early stages of unloading, dead rats were uncovered which, on bacteriological examination, were found to be infected with plague. Unloading was stopped and on my advice the vessel was fumigated throughout with hydrogen cyanide, the bulk of the cargo being still on board. After prolonged ventilation, unloading was completed and the vessel again fumigated. Two hundred and twenty-six dead rats were found after the first fumigation and five after the second, the inference being that the first fumigation had much reduced the risk of plague-infected rats escaping from the ship to the shore.

As another example the case of the S.S. "Somali" may be quoted. This vessel arrived in the Port of London on July 1, 1937, from the Far East with a mixed cargo. Two hundred rats were stated to have been caught during the voyage although the vessel was in possession of a deratization certificate issued at Kobe on April 28 following fumigation of the partly unloaded vessel with a mixture of carbon monoxide and carbon dioxide. An unusual mortality amongst the rats on board was discovered whilst the cargo was being discharged at a pontoon, and specimens sent for bacteriological examination on July 5 suggested the presence of plague infection. The unloading of the cargo was accordingly stopped and the vessel was fumigated throughout with hydrogen cyanide, the remainder of the cargo being discharged into lighters. As a result of the fumigation no less than 420 rats were recovered and after the unloading had been completed the vessel was again fumigated with hydrogen cyanide when a further 103 dead rats were found. The loaded barges into which the cargo had been discharged were also fumigated with hydrogen cyanide.

In the following year the Ministry of Health issued a Memorandum (revised in 1937) on the fumigation of ships with hydrogen cyanide and the procedure necessary to ensure success and to avoid accident. The Mercantile Marine Department of the Board of Trade also issued a notice (No. 94 of 1928) to shipmasters based on the Ministry's Memorandum.

The Health Committee of the League of Nations and the Permanent Committee of the Office International d'Hygiène publique also set up an expert Commission on the fumigation of ships under the Chairmanship of Surgeon-General Cumming to study in detail some of the problems arising in connexion with the fumigation of ships with hydrogen cyanide and more particularly the fumigation of ships in cargo. The more important conclusions of this Commission were: That the time had not yet arrived when one particular method for the fumigation of ships to the exclusion of all other methods could be recommended, but that the indiscriminate spraying of liquid HCN should not be practised and that neither the liquid acid nor other forms of cyanide should ever be poured directly on to bedding, carpets, &c. If carefully carried out, the fumigation of a loaded ship with HCN by the methods in use would account roughly for 80% of the rats, but various expedients must be adopted to reach rat harbourages in the lower parts of a ship under the cargo. The Commission recorded that no indications had been obtained of any injury to health or of deterioration of food values resulting from the consumption of fumigated food, but further investigations were desirable. With regard to the danger to fumigators working with high concentrations of HCN, they recommended that an oxygen breathing apparatus should be used instead of a gas mask.

Finally, the Commission pointed out that the problem of reducing the number of rats on shore merited the special consideration of Sanitary Authorities of seaports and seaport towns throughout the world, and that if the rat-proofing of ships really make it easier for ships to obtain exemption from fumigation they believed that shipowners would co-operate and that world shipping would become less and less a breeding ground for rats (*see also* Ref. 5).

The possibilities of rat-proofing continued to receive attention in the United States and the publication of an article on the rat-proofing of vessels in the Public Health Reports for July 17, 1925, aroused such widespread interest, especially among shipbuilders and shipowners, that the article was translated subsequently into several languages. A second and larger edition was published in December 1926.

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Port Health Authorities generally adopted the word "PORTELTH" as their telegraphic address.

The meaning of the old visual signals was also changed and the flag signal "Q"—the yellow flag—no longer indicates that the vessel is in quarantine, but means: "My ship is healthy and I request free pratique!"

New arrangements were laid down for establishing "mooring-stations" where "infected" or "suspected" vessels can be detained and dealt with, it being made obligatory that one at least should be within the Docks. The Port Health Officer can, however, with the concurrence of the Customs, designate special "mooring-stations" and is thus able to arrange for a vessel being isolated and dealt with at her ordinary berth—as indeed is commonly done.

Provision was also made for the approval of suitable ports for the issue of International Deratization and Deratization Exemption Certificates and the approximate numbers of such certificates issued, during recent years, at the 24 "Approved Ports"¹ in England and Wales with the method of deratization employed, are shown in the following table:

APPROXIMATE NUMBER OF DERATIZATION AND DERATIZATION
EXEMPTION CERTIFICATES ISSUED DURING 1933-1945.

Year	HCN			HCN and sul-phur		Sal-for-kose	Trapping and poison-ing	Exemption		Total issued
	Li- quid	Zylon B	Other meths.	Sul-phur	sul-phur			No. issued	%	
1933	375	81	22	648	5	2	19	1152	4261	70
1934	357	96	30	615	2	5	25	1130	4526	80
1935	244	77	8	613	3	8	23	976	4442	82
1936	251	72	14	608	6	7	31	989	4584	82
1937	232	112	18	562	3	5	27	959	4774	83
1938	243	124	24	462	11	1	6	871	4467	84
1939	192	113	13	388	10	3	8	727	4168	85
1940	164	99	31	351	14	3	18	680	3735	85
1941	191	135	20	311	10	1	11	679	2334	77
1942	282	248	8	138	26	—	12	714	1645	70
1943	434	273	8	66	21	—	17	819	1486	65
1944	527	304	5	60	7	—	13	916	1407	61
1945	669	354	45	40	20	—	26	1154	2035	65

With improvements in methods of fumigation, Port Health Authorities are finding that they are able to fumigate vessels while loaded with a reasonable prospect of destroying most of the rats on board, though this depends to a great extent on the nature of the cargo and its stowage in the holds. Many Authorities do not hesitate to fumigate before unloading if they fear that a ship may present a risk of the transfer of plague-infected rats ashore. In such cases the Quarantine Commission of the Paris Office expressed the view (in 1934) that only one of the fumigations should be at the charge of the ship, any subsequent fumigation being a charge on the port. This practice of repeated fumigations was not envisaged in the International Sanitary Convention of 1926 and its regularization will necessitate an amendment to the text of article 25—which is under consideration. In Great Britain "Bills of Health" have not been required for many years, but it is of interest to note that two parallel international agreements for the abolition of the Bill of Health and of the Consular visa thereon were drawn up by the Office International in 1934. It is quite anomalous that, though aeroplanes are not required to carry Bills of Health, some countries still demand them from the comparatively slow-moving ship. Under the International Sanitary Convention of 1944, however, Bills of Health and Consular visas are to be abolished "as soon as the conditions of hostilities permit the establishment of effective epidemiological communications".

Only a few other advances in Port Health Administration can be listed. In order that smallpox contacts proceeding abroad (before the incubation period of the disease has elapsed) might be kept under surveillance, the Ministry issued a circular (No. 1021) in 1929 asking that the requisite information in such cases should be furnished to the Ministry, who would then notify the appropriate Public Health Authority abroad. Similarly, a circular (No. 1171) was addressed to Port and Riparian Sanitary Authorities in 1931 regularizing the practice which was growing up of communicating any essential information, in regard to "infected" or "suspected" ships, by the port of arrival to the next port of call.

Arrangements were also made with Shipping Companies, the French Administration and our Consul-General at Marseilles for facilitating surveillance in this country of any contacts who land from vessels calling at Marseilles and proceed overland to one of the Channel Ports.

Under the International Sanitary Convention of 1926, the signatory countries agreed to keep one another informed, through the Office International, of the measures taken

¹ Barrow-in-Furness; Barry; Blyth; Bristol; Cardiff; Dover; Falmouth; Fowey; Grimsby; Hartlepool; Hull; Immingham; Liverpool; London; Manchester; Middlesbrough; Newport; Plymouth; Southampton; Sunderland; Swansea; Tyne; Weymouth; Workington; and the three naval ports: Chatham, Devonport and Portsmouth.

Following the consideration of this report the Office International issued provisional standards for the fumigation of vessels, and in 1931 the Ministry of Health issued a circular (No. 1194) to Port and Riparian Sanitary Authorities on Plague Preventive Measures. This circular emphasized the need for being constantly on the watch, for continuously applying measures for rat destruction and the elimination of harbourage and for Port Health Authorities keeping themselves regularly informed of the condition of the rats in the ports by frequent and systematic examination.

In this connexion the rat-flea survey carried out in the Port of Cardiff and described in Dr. Greenwood Wilson's Annual Report for 1934 is of particular interest.

The prevention of the landing of rats from a vessel known or suspected to be infected with rodent plague is one of the most serious problems with which Port Health Authorities are faced. The use of rat-guards was raised at the Office International d'Hygiène publique who, after considering the replies to a questionnaire sent to the various countries participating in the Office, concluded that:

(1) Rat-guards are only effective if they are suitably constructed, and if certain specific conditions are observed in regard to their application. In practice, the strict observance of these conditions presents so many difficulties that the Commission can only competently recommend the use of rat-guards if there is a real danger of the introduction of rat plague, which justifies the necessity for taking all possible measures for preventing the passage of rats.

(2) At present it is hardly possible to recommend the adoption of a uniform standard type of rat-guard, but certain principles, in regard to their construction, should be kept in view.

The Commission also suggested that further experiments should be made with the electrical type of guard and these were carried out at Bristol, Hull and Liverpool under the auspices of the Association of Port Sanitary Authorities, but in the report presented by Dr. Frazer, the conclusions were that the electrical type of rat-guard was not suitable for use at the ports in this country.

The recent appearance of human psittacosis led the permanent Committee of the Office International d'Hygiène publique to consider in 1930 the question of harmonizing the action taken by different countries to prevent the importation of parrots and the Parrots (Prohibition of Import) Regulations 1930 added a new responsibility to Port Medical Officers of Health.

To return to the story, the International Sanitary Convention of 1926 was finally implemented by the Port Sanitary Regulations of 1933, which came into force on May 1 of that year. Similar Regulations, which came into operation on the same date, were also issued by the Department of Health for Scotland and the Ministry of Home Affairs for Northern Ireland. Only a few modifications were necessary when the International Sanitary Convention of 1944 was implemented and as the Regulations are still in force—and indeed have well stood the test of time—only the salient points need be mentioned.

The aim of the regulations, which are partly administered by the Customs, was to give further effect to the obligations assumed under the 1926 Convention and to consolidate in one code the various then existing Regulations—such as the several general and special Cholera, Yellow Fever and Plague Regulations of 1907, the Port Sanitary Authorities (Infectious Diseases) Regulations, 1920, and the Public Health (Deratization of Ships) Regulations, 1929—which were revoked.

They provide for wireless messages from incoming vessels from foreign, the obligation of hoist signals¹ indicating the state of health on board (which the Master must ascertain before arrival) and the obligation on the Master to make a written Declaration of Health (which must be countersigned by the Ship's Surgeon, if one is carried).

With the advances made in the use of wireless after the 1914-18 war, radio messages were being more and more utilized as a means of communication between incoming vessels and the shore and the system introduced at Plymouth proved so successful that in the new Regulations, powers were given to the Minister to designate ports to which approaching ships (if fitted with suitable transmitting apparatus) must send a wireless message if there were infectious disease on board. To simplify the sending of the messages

¹ *International Code of Signals*.—Codes of signals for the use of mariners have been published in various countries since the beginning of the 19th Century. The best known is Captain Marryat's, which was published in 1817 and was probably the first international code. Various revisions were made and during the 1914-18 war the code drawn up in 1897 was in use, but broke down under war conditions. After the war, revision was undertaken at the suggestion of the British Government, first by the International Radiotelegraphic Conference at Washington in 1927 and later completed, at the request of this Conference, by the British Government with representatives of each of the governments concerned in 1931. The new code was compiled in two volumes, one for use by radiotelegraphy and the other by visual signalling: the British Edition being published in 1932. The code for radio signalling contains a complete medical section and a code for accelerating the granting of pratique which were inserted with the assistance and by the advice of the Office International d'Hygiène publique. Another feature of the new code is the introduction of words and phrases applicable to aircraft. Nautical and technical expressions have been adjusted in the seven editorial languages so that the use of the code will facilitate the exchange of correct and concise information between people not speaking the same language.

The progress of aviation, however, since the Wright Brothers made their first flight in 1903 and Bleriot flew the Channel in 1909, created new problems. An International Convention relating to the Regulation of Aerial Navigation was drawn up in 1919 the year the Atlantic was first flown by Alcock and Brown. Gradually it was recognized that the very speed of air traffic and the opening up of new air routes between country and country might produce special dangers of their own. This was notably the case with the establishment of regular air communications between countries in which yellow fever might exist and those countries which, though they have never known the infection of yellow fever, contain both susceptible populations and the species of mosquito by which the infection is carried from man to man. As a result the Office International d'Hygiène publique in 1930 drafted an International Sanitary Convention for Aerial Navigation which was so framed as to take full account of the special conditions of aircraft and of the circumstances in which they might be more, or less, likely than are ships to convey infection from country to country. The final text was opened for signature at the Hague in April 1933, but this convention has not been as widely accepted as the "Maritime" Convention of 1926. It was only signed by 23 countries, of whom 16 subsequently ratified but Bolivia, Brazil, Chile, Irak, the Soudan, Southern Rhodesia and a number of British Colonies and Protectorates afterwards adhered.

Briefly the Convention, which applies only to aircraft which pass from one territory to another, lays down the measures which may be taken for the control of infectious diseases introduced by aircraft and those which in cases of necessity must be taken to prevent the exportation of such diseases. Three classes of aerodromes are defined, viz:

- (i) Customs (or authorized) aerodromes.
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- (iii) Anti-amaryl aerodromes (in yellow fever areas) where mosquito-proof dwellings must be provided and persons can be subjected to observation for six days (to cover the incubation period of yellow fever). Other special precautions must also be enforced against mosquitoes.

When the Convention came into force there were 11 Customs aerodromes for the use of land-planes, four for sea-planes and one for the use of airships. These came under medical control by the Local Authority as legislation was then necessary before Regulations to implement the Convention could be finally drafted.

The Public Health (Aircraft) Regulations came into force on July 1, 1938, and are applicable to all aerodromes or places approved by the Commissioners of Customs for the landing or departure of foreign-going land-planes or sea-planes.

Twenty-four aerodromes were then approved as "Customs" aerodromes. Four of these, i.e. Doncaster, London (Croydon), London (Heston) and Southampton Water were designated by the Minister as Sanitary Aerodromes and the Office International d'Hygiène publique was duly informed in accordance with the terms of the International Sanitary Convention for Aerial Navigation.

The object of the Regulations was to prevent the introduction of infectious disease into the country by air-borne traffic which was rapidly increasing. They are administered (i) by Port Health Authorities, if the aerodromes or places for the landing of aircraft are within their district; (ii) by the local authority, including a county council, that maintains an aerodrome; and (iii) in respect to other aerodromes by the local authority of the district in which the aerodrome is situated. No grant has been payable but the cost of the medical inspection of aliens is met by the Exchequer.

When the Regulations came into force, the bulk of the traffic was dealt with at Croydon and Heston, whilst the long distance sea-planes of the old Imperial Airways used the Marine Airport at Southampton. The landing there of a doubtful case of cholera from India in August 1938, led Dr. Maurice Williams to introduce a simple form of "declaration of health" which materially assisted the arrangements for the surveillance of travellers arriving by air from countries where the more dangerous infectious diseases were present. Incidentally, about the same time, American Authorities introduced a "declaration of origin" from passengers coming from an area infected with yellow fever in the form of a statement of their movements during the six days previous to landing. When the International Sanitary Convention for Aerial Navigation of 1944 was drawn up these two forms were amalgamated into the Personal Declaration of Origin and Health form which, under this Convention, is demanded from passengers arriving on aircraft.

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As far back as 1911 the congress of the Royal Sanitary Institute urged a thorough revision of the requirements in respect of the living quarters for officers and men of all new vessels and the Association of Port Sanitary Authorities made detailed recommendations in 1922 and again in 1935. It is therefore particularly satisfactory to record that in 1937 the Board of Trade issued new Instructions as to the survey of Masters and Crew spaces, based on more modern standards, which have gone a long way to remedy in new ships the old defects. Whilst nuisances on ships are usually dealt with by the officers of the Port Sanitary Authority, defects of construction and structural alterations are matters for the Board of Trade surveyors, the relative responsibilities being indicated in a circular (No. 1670) issued by the Minister in 1938 when forwarding copies of the revised Board of Trade instructions.

With the outbreak of the World War in 1939, new responsibilities devolved on Port Medical Officers of Health in connexion with Civil Defence. Crowds of refugees arrived and ports such as Dover and Harwich were taken over by the Admiralty for naval purposes, and traffic from many ports was diverted owing to enemy action and the introduction of the convoy system. Owing to the war, vessels had to change their routes and an increasing number of cases of malaria began to occur on arriving vessels. More and more ships on the way home were calling at Freetown and other West African ports, where malaria was being contracted.

Port Medical Officers of Health were circulated and asked to keep the possibility of malaria constantly in mind when examining sick persons on ships arriving from foreign and specially those which had called at West-African ports and to forward to the Ministry particulars of all vessels on which malaria had occurred during the voyage.

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As the war progressed much strain was thrown on many ports whose normal staff had already been depleted by the call to the Armed Forces but the history of the War Years yet remains to be written.

One reform, however, which was long overdue, was finally accomplished. To meet the views of the Association of Port Sanitary Authorities, the designation was changed to Port Health Authorities by the Public Health Act of 1936, but there were difficulties then in effecting the consequential amendment in the title "Port Sanitary Regulation". When it became necessary to give effect to the provisions of the International Sanitary Convention of 1944, the anomaly was corrected in the Port Health Amendment Regulation of 1945, and our sea ports at last have Port Health Authorities and Port Health Regulations.

II. AIR TRAFFIC

In reviewing the progress of Port Health Administration much attention has of necessity been devoted to maritime traffic.

The progress of aviation, however, since the Wright Brothers made their first flight in 1903 and Bleriot flew the Channel in 1909, created new problems. An International Convention relating to the Regulation of Aerial Navigation was drawn up in 1919 the year the Atlantic was first flown by Alcock and Brown. Gradually it was recognized that the very speed of air traffic and the opening up of new air routes between country and country might produce special dangers of their own. This was notably the case with the establishment of regular air communications between countries in which yellow fever might exist and those countries which, though they have never known the infection of yellow fever, contain both susceptible populations and the species of mosquito by which the infection is carried from man to man. As a result the Office International d'Hygiène publique in 1930 drafted an International Sanitary Convention for Aerial Navigation which was so framed as to take full account of the special conditions of aircraft and of the circumstances in which they might be more, or less, likely than are ships to convey infection from country to country. The final text was opened for signature at the Hague in April 1933, but this convention has not been as widely accepted as the "Maritime" Convention of 1926. It was only signed by 23 countries, of whom 16 subsequently ratified but Bolivia, Brazil, Chile, Irak, the Soudan, Southern Rhodesia and a number of British Colonies and Protectorates afterwards adhered.

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JOINT DISCUSSION No. 3

Section of Neurology with the Section of Radiology

Chairman—J. PURDON MARTIN, M.D., F.R.C.P.

(President of the Section of Neurology)

[February 15, 1946]

RADIATION TREATMENT OF CEREBRAL TUMOURS

Dr. R. McWhirter: The following investigation into the radiosensitivity of brain tumours was undertaken in association with the Department of Surgical Neurology and I should like at the outset to acknowledge its most helpful co-operation in the investigation and in the preparation of this Address.

Ten years ago our knowledge of the radiosensitivity of the different forms of brain tumour was restricted. Accordingly when this investigation was begun in 1936 it was decided that wherever possible the exact histological nature of the tumour to be irradiated would be determined and that all cases would be carefully followed up.

Cases selected for consideration.—All cases histologically proven and treated by radiotherapy as part of the first planned method of treatment during the period 1936 to 1944 have been included.

In a number of cases the X-ray treatment was incomplete either because of deterioration in the patient's general condition or because the tumour was obviously radio-insensitive. All such cases have, however, been included in the following tables, for their omission would give an erroneous impression of the value of radiotherapy.

All deaths have been assumed to be due to the tumour. Of the total 115 cases 4 have not been fully traced, making the percentage of cases lost sight of 3.5%.

Spongiblastoma polare has been included with the astrocytomas and the astroblastoma with the glioblastomas.

TABLE I.—ALL HISTOLOGICALLY PROVEN BRAIN TUMOURS, 1936-1944.

	Total	No. treated by X-rays
Astrocytomas	61	7
Ependymomas	8	4
Oligodendrogliomas	5	5
Meningiomas	74	33
Hamangioblastomas	15	10
Neuro-epitheliomas	2	2
Medulloblastomas	19	13
Ependymoblastomas	17	11
Malignant choroidal papillomas	6	3
Pinealoblastomas	11	2
Glioblastomas	106	25
Total	324	115

Following consideration of the above group of tumours, a brief comment will be made on the tumours of the pituitary region and on spinal tumours.

Method of treatment.—The extent of the surgical treatment has varied. In 5 out of the 115 cases the tumour was apparently completely removed, but because complete removal could not be guaranteed radiotherapy was given later. In the remainder only a partial removal of the tumour was undertaken or only sufficient tissue was removed for histological examination.

In the majority of cases a decompression was carried out so that the tumour could be accurately localized and its extent determined. Where there was interference with the fluid circulation, sufficient tumour tissue was removed to overcome this. When cysts were present these were opened to diminish the bulk of the tumour. Decompression also permitted of inspection of the gross appearance of the tumour and, as will be shown later, this is of considerable importance in the selection of the meningiomas likely to be suitable for radiotherapy.

From the data of clinical neurology, air ventriculography and operation findings, the position and the extent of the tumours were assumed and were marked on anterior and lateral radiographs and the patient sent for radiotherapy.

The X-ray treatment has naturally undergone some modification over the period but in general patients were treated by X-rays generated at 250 kV. and filtered by a Thoracufilter. Two directly opposed fields centred over the tumour were used and each field was treated every day. A minimum tumour dose of 4,500 r in four weeks was planned but, as already indicated, this dose level was not reached in a number of cases.

Following the outbreak of the war, ordinary civilian air traffic gradually decreased and aerodromes came more and more under R.A.F. control. The difficulties of proper surveillance of passengers arriving by air also increased and arising out of a suggestion by Dr. Chesney—the Port M.O.H. of Poole—Dr. Goodman and Mr. Dark of the Ministry of Health drew up a card which is now handed to each passenger from abroad when he arrives, on which is printed a notice in English and French warning him that while abroad he may have been in contact, without knowing it, with some dangerous infectious disease and urging him at once to consult a doctor and to show him the card should he fall ill within twenty-one days of arrival. On the reverse side of the card the attention of the doctor is drawn to the fact that his patient has been abroad and he is asked, if infectious disease is found or suspected, at once to notify the Medical Officer of Health and inform him of the date and airport (which is given on the card) of the patient's arrival. These particulars will help in locating other passengers who travelled on the same plane and the taking of other precautions.

As smallpox is now the chief danger to be apprehended the original card is being revised to stress this disease and incidentally the Services have introduced a "warning-card" which is handed to their personnel who have travelled on ships on which smallpox has occurred during the voyage.

To what extent this system will obviate the necessity of placing unprotected travellers from infected areas under surveillance it is difficult to judge, but the underlying idea of getting each passenger to carry out his own surveillance is being given an extended trial.

III. THE UNRRA CONVENTIONS

Towards the end of 1943, when the United Nations Relief and Rehabilitation Administration was formed, one of the main aims was to provide aid in the prevention of pestilence. Fears were then expressed of the danger of epidemics in the liberated countries and as Paris was then in enemy hands and no help could be obtained from the Office International d'Hygiène publique, an expert Commission on Quarantine was set up, the terms of reference being to consider the scope of the existing International Sanitary Conventions and to draft any necessary amendments of an emergency nature taking into account the progress of medical knowledge since the 1926 and 1933 Conventions were prepared—particularly in regard to yellow fever and the increasing speed of air travel. As a result, two new International Sanitary Conventions came into force on January 15, 1945 (UNRRA becoming the international body responsible for administering them for the time being), viz.: the International (Maritime) Sanitary Convention of 1944 amending the International Sanitary Convention of 1926, which has been implemented by the Port Health Amendment Regulations of 1945, and the International (Aerial) Sanitary Convention of 1944 amending the International Sanitary Convention for Aerial Navigation of 1933. This latter Convention has not yet been fully implemented as legislation is awaited in connexion with the recently formed Ministry of Civil Aviation. Particulars of these Conventions have, however, already been communicated to this Section [13].

Before concluding this outline of Port Health Administration, during the period which practically coincides with the life of this Section of the Royal Society of Medicine, I should be lacking in appreciation if I did not pay my tribute to the work of Port Medical Officers and their staffs. To have given a fuller account of the many duties they now carry out would be impossible in a single paper. The work calls for initiative and quick decision. To wait on a dirty night, in a tossing launch, for the ship which may be delayed, to climb the rope ladder and then make the right diagnosis in the minimum of time requires pluck, character and skill. Wireless telephony should gradually lessen the difficulties of the boarding officer but that so few mistakes have been made in the past twenty-five years is a greater tribute to the efficiency of the Port Health Service than any I could voice and one which would delight the heart of Richard Reece were he with us to-day.

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- 13 STOCK, P. G. (1945) *Proc. R. Soc. Med.*, 38, 309-316.

degree of accuracy the radiosensitive tumours from the radio-insensitive tumours and has made the following observations:

"Meningiomas with extensive hyperostosis are sensitive. Meningiomas, where the blood supply is mainly dural, are insensitive. Those with a cerebral blood supply are sensitive (excluding the intraventricular types). The meningiomas of multilobular form with a smooth firm oedematous cortex and soft pale interior within the lobules, with the larger blood-vessels on the surface and in the septa between the lobules are sensitive. The firm solid tumours with a granular surface and with vessels evenly distributed throughout a tough homogeneous substance are insensitive. Most of the meningiomas *en plaque*—both the soft and the pale hard avascular types—are sensitive.

"In a group of 82 meningiomas 22 cases (or 27%) were proved to be radiosensitive, 10 (or 12%) were proved to be radio-insensitive. A further 13 (or 16%) have been assumed to be radiosensitive. This makes a total of 43% of the meningiomas suitable for treatment by X-ray therapy."

(3) *The radiosensitive metastasizing tumours:*

TABLE IV.

		Years after treatment	Exposed to risk	qx	Survival rate %
Medulloblastomas ...	13	0	29	0.2069	100
Ependymoblastomas ...	11	1	21	0.2857	79.31
Malignant choroidal papillomas	3	2	19	0.5000	56.65
Pinealoblastomas ...	2	3	5	0	28.32
		4	4	0.5000	28.32
Total admissions	29	5	—	—	14.16

The five-year survival rate in this group is 14%.

All the tumours in this group are highly radiosensitive and little difficulty was experienced in the destruction of the main primary tumour mass. Failure to cure the patient was due to the fact that these tumours have a marked tendency to metastasize to other parts of the cerebrospinal axis, and, in particular, to the basal cisterns and to the spinal canal.

The method of treatment in this group has now been changed and localized treatment has been replaced by extensive fields arranged so as to include the whole of the cerebrospinal axis. The best method of treating this large area is still under investigation and has not yet been finally determined.

(4) *The ? radiosensitive tumours:*

TABLE V.

		Years after treatment	Exposed to risk	qx	Survival rate %
Glioblastomas ...	25	0	25	0.4400	100
		1	14	1.0000	56.00
Total admissions	25	2	0	—	0
		3	0	—	—
		4	0	—	—
		5	—	—	—

The glioblastomas have been placed in a separate category. Thus, while at present the application of X-radiation to glioblastomas is of doubtful value, there is evidence that some of these tumours are not entirely unresponsive, and we propose to keep an open mind regarding future possibilities as radiotherapeutic technique may improve in tumour lethal potency and neoplastic selectivity.

All the histologically proven tumours:

TABLE VI.

		Years after treatment	Exposed to risk	qx	Survival rate %
(1) Radio-insensitive tumours ...	23	0	114.5	0.2009	100.0
(2) Radiosensitive non-metastasizing tumours ...	34	1	81	0.3457	79.91
		2	42	0.2143	52.20
(3) Radiosensitive metastasizing tumours ...	29	3	26.5	0.0755	41.08
		4	14	0.2357	37.93
(4) ? radiosensitive tumours ...	25	5	—	—	27.13
Total admissions	115				

The five-year survival rate of all cases is 27%.

With the increased knowledge now available cases will be more carefully selected for X-ray treatment, and, if a suitable method of treatment can finally be elaborated for the radiosensitive metastasizing tumours (Group 3) the results in the future will probably show considerable improvement.

Pituitary tumours.—Only a brief comment will be made for the main object of this paper has been to present the findings in the group of tumours already discussed.

Chromophobe adenomas are no longer treated by radiotherapy for no conclusive evidence of their response to treatment has been obtained. In assessing the value of radiotherapy it must be borne in mind that spontaneous arrest of growth for indefinite periods and even spontaneous retrogression are in fact not uncommon.

The eosinophil tumours are suitable for treatment by X-ray therapy. In the majority of cases the rate of advancement of the acromegaly is slowed down and in some cases definite improvement may be obtained. Further, the bulk of tumour may significantly

Assessment of the effect of radiotherapy.—It is always difficult to assess accurately the precise effect of radiotherapy on any tumour which cannot be directly inspected during the whole course of treatment and subsequently. The following observations are based mainly on the clinical assessment of the size of the tumour as a space-occupying mass, in terms of its effect on cerebral function and in terms of brain plus tumour volume as judged from fullness or recession at cranial defects. In some cases still more accurate assessment has been possible. Further operations have been undertaken in a number of cases (in particular in the meningiomas proved to be insensitive) and the gross appearances and the histological findings after treatment have been compared with those of the original operation. A post-mortem examination has been obtained in a number of cases. In others X-ray examination has provided useful information. Thus subsequent ventriculography may show the absence or persistence of the mass. In one case where fine specks of calcification were present throughout the tumour it was possible to follow the shrinkage of the tumour during treatment to the final stage where the calcification was reduced to a thin plaque.

From the above observation it has been possible to classify the brain tumours into four main groups:

(1) *The radio-insensitive tumours:*

			TABLE II.	Exposed	qx*	Survival
			Years after treatment	to risk		rate %
Astrocytomas	7	0	22.5	0.1778	100
Ependymomas	4	1	16	0.4375	82.22
Oligodendrogliomas	5	2	8	0.3333	46.25
Radio-insensitive meningiomas		7	3	6	0.1667	30.83
			4	2	0	25.00
			5	—	—	25.00
Total admissions	23					

*qx is the probability or chance of dying in any one year.

It will be seen from the table that 26% of the patients in this group are alive at the end of five years.

The astrocytomas, the ependymomas and the oligodendrogliomas are all slowly growing tumours and patients with these tumours may survive for more than five years with no treatment at all. In assessing the value of radiotherapy, therefore, the survival rate is of little value. The survival rate in the above group did not differ materially from cases receiving no radiotherapy. There was no clinical proof that the tumour mass had diminished in size and where subsequent operation was carried out the tumour was unaltered.

The meningiomas will be considered more fully in the next section where it will be shown that from the radiotherapeutic point of view there are two types of meningioma—one radiosensitive and the other radio-insensitive. The radio-insensitive tumours are, of course, included above. When the tumour was found to be radio-insensitive subsequent operation was performed in a number of cases and the tumour removed. The absence of radiation effect upon its bulk and its component cells was then verified.

From what has been said it will be appreciated that the five-year survival rate of 26% is due to the naturally slow growth of the first three tumours and to the mechanical gains from partial tumour removals and from decompressive effects. It is possible that while radiotherapy did not cause diminution in the tumour bulk it may have slowed down the rate of growth of these tumours. The subsequent total surgical removal of some of the meningiomas has also influenced the five-year survival rate.

(2) *The radiosensitive non-metastasizing tumours:*

			TABLE III.	Exposed	qx	Survival
			Years after treatment	to risk		rate %
Radiosensitive meningiomas	26		0	38	0.0526	100
Hæmangioblastomas ...	10		1	30	0.0333	94.74
Neuro-epitheliomas ...	2		2	23	0.0435	91.53
			3	15.5	0.0645	87.60
			4	8	0.2500	81.95
			5	—	—	61.49
Total admissions	38					

This group has given the best results and it will be seen that the five-year survival rate is 61%.

The radiosensitive meningiomas form the biggest group. That some meningiomas were radiosensitive was recognized as early as 1936 and it is of considerable interest to record that so far it has been impossible from histology alone to differentiate between the radiosensitive and the radio-insensitive meningiomas. The average duration of symptoms before treatment in the radiosensitive group is about two years and about five and a half years in the radio-insensitive group, but the figures for individual cases have too wide a variation to permit of the duration alone being used as a means of differentiating between the two types. From his clinical experience and from the gross anatomical appearances at the time of operation Mr. Dott can distinguish with a fair

degree of accuracy the radiosensitive tumours from the radio-insensitive tumours and has made the following observations:

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		4	14	0.2857	37.98
		5	—	—	27.13
Total admissions	115	—	—	—	—

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Total admissions	38			4	8	0.2500
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symptoms for a very long time, and if a course of radiation treatment is given there is no way of saying what effect it has had on the tumour. We have one or two cases of oligodendroglioma which have not had a decompression but have been treated with radiation through the intact skull, and they have remained fairly well for periods of three or four years. We have also had some cases of astrocytoma of the basal ganglia which have had simple decompressions followed by radiation treatment with survival periods of three or four years. These tumours are, to some extent, radiosensitive and worth treating.

Three cases of meningiomata have been treated by radiation therapy, one in the cerebellopontine angle, one on the upper and posterior surface of the petrous bone, and one in both frontal regions, and only in the last case has there been any improvement. This was a very vascular tumour, with vascular channels in the skull the size of one's little finger, and the patient, a middle-aged woman, became repeatedly exsanguinated at repeated operations to expose and partially remove the tumour. Now after two years and one course of deep therapy, the decompression area is indrawn and she is free from symptoms. However, we have not done a ventriculogram to see whether, or how much, tumour remains.

Our results with the cerebellar medulloblastoma do not differ significantly from those previously published. Our best case looks like being that of a young adult who had a tumour of the upper vermis extending into the left cerebellar lobe completely removed in September 1942. It was thought at operation to be an ependymoma, but histological examination left no doubt that it was a characteristic medulloblastoma. He was thus given a course of deep therapy following operation, and to date there has been no sign of recurrence. One wonders whether we should not more often try to effect a wide removal of these tumours and follow this with a course of radiation treatment—although in those cases in which the floor of the fourth ventricle is involved, or in which there are already meningeal metastases, surgery probably has little to offer.

The cerebellar ependymoma, a tumour which usually grows in the lower part of the fourth ventricle, is often attached to the floor or to the calamus scriptorius, and presents as a mass in the cisterna magna. These are essentially benign tumours, but their situation usually means that complete removal is not possible without doing irreparable damage to the medulla. It has been the experience of most people, however, that a subtotal removal, leaving a fringe of attachment to the calamus will keep these patients free from symptoms for a number of years, if not permanently.

In November 1939 we admitted a little girl aged 7 with a short history of headache, vomiting, unsteadiness in walking, which symptoms confined her to bed within two or three weeks. On examination, there was no enlargement of the skull, intense papilloedema, nystagmus to both sides, ataxy of all four limbs, with in the lower limbs a considerable flaccid weakness and absence of tendon reflexes, sphincteric paralysis, and a good deal of pain in the back. Clinically this looked like a medulloblastoma with spinal metastases. A ventriculogram indicated a tumour in the lower part of the fourth ventricle and she was given a trial course of deep therapy. The result was immediate and dramatic, and was regarded as confirming the diagnosis. Within four or five weeks she had regained her normal health, and it was not possible to demonstrate any neurological abnormalities. She had a relapse about a year later, and again a course of treatment brought about this dramatic improvement. She finally died in a third relapse in December 1943, four years after the onset of symptoms, and at autopsy we found a characteristic ependymoma.

It may be a good idea to give a course of treatment as a routine in these cases.

Have we really any evidence that radiation treatment has an effect on brain tumours? I think anyone who has seen the response of a medulloblastoma to a course of X-ray therapy would say yes. But even with these tumours it is a prolongation of life and not a cure which we achieve. Are brain tumours ever cured by radiation? We have experience of one case in which the answer to that, too, is in the affirmative.

In April 1935 a young woman was admitted to the National Hospital, Queen Square, under the care of Dr. Critchley. She had been in good health until two months before admission when, after a mild attack of influenza, she began to complain of progressively severe headache and vomiting, and she had two epileptic attacks characterized by turning of the head and eyes to the left side, and convulsive movements of the left side of the face and left upper limb. After the second of these there was a progressive weakness of the left side of her body. On examination there was bilateral papilloedema, and a slight but definite weakness of the left limbs and face, with a corresponding alteration in the reflexes. X-rays of the skull were normal, but the spinal fluid pressure was elevated and the fluid contained an excess of protein. There was thus little doubt that there was an expanding lesion in the right frontal region, either a rapidly growing glioma or possibly an abscess. At operation Mr. Hugh Cairns found a subcortical glioma in the right frontal lobe. Sufficient of this was removed for histological examination and Dr. Greenfield demonstrated that it was a glioblastoma multiforme, of a malignant type. There was some improvement after operation, notably in the relief of headache and subsidence of papilloedema, but little alteration in the left-sided weakness. Four weeks after operation a course of radium treatment was given, 44,400 mg.-hrs. (100 mg. plaque) directed to the right frontal region.

decrease as evidenced by improvement in visual field defects and other signs of local pressure effects.

In Cushing's syndrome where the cause is a basophil pituitary tumour very striking results may be obtained. It always remains difficult, however, to identify those cases where the syndrome is actually due to a basophil pituitary tumour.

Craniopharyngeal carcinoma (pharyngeal endothelioma)—the invasive tumour of the base of the skull which appears to be a primitive type of carcinoma akin to branchial carcinoma is highly radiosensitive and good results have been obtained over a number of years of observation.

Spinal cord tumours.—The response is similar to that found in the cerebral tumours with the exception that the spinal cord meningiomas all appear to be radio-insensitive.

Mr. J. Pennybacker: The difficulties of assessing the value of radiation are greater in the case of brain tumours than with tumours in most other parts of the body. We cannot see these tumours to know whether they are increasing in size or shrinking, and attempts at indirect visualization, e.g. by repeated ventriculograms, are often not practicable. Usually a person who is sent for radiation has had some kind of cranial operation, and it is difficult to say how much of immediate benefit results from the surgical procedure, which may be nothing more than a decompression, and how much is attributable to radiation therapy. It would appear that a comparison of survival periods in comparable types of tumour, one group of which had been treated only surgically, and the other by surgery with subsequent radiation, would give some valuable information. Dr. Francis Schiller in our department has recently attempted such an analysis, but even with some 200 cases of verified tumours the individual groups were too small to be of statistical significance. At present most of us rely on impressions, and on the memory of occasional outstanding cases which seem to have responded favourably. More frequently we resort to this kind of treatment because we realize that we are dealing with a problem which is beyond the scope of radical surgery, and I believe this includes most gliomata which constitute the majority of brain tumours.

In selecting cases for radiation treatment, we try to verify histologically every brain tumour, either by open exploration or by needle biopsy. This we regard as of the utmost importance, as on a number of occasions patients who have presented the clinical features of malignant gliomata have proved to have benign and remediable lesions, such as a meningioma, abscess or subdural hæmatoma. No amount of wisdom and neurological experience can make this differentiation as accurately as the surgeon at operation and the pathologist with his microscope. If the tumour proves to be a benign one in an accessible situation we try to remove it, even though we may add slightly to the patient's disability in so doing, by which I mean that a person with focal epilepsy due to a parasagittal meningioma may have his tumour out, but be left with a slight weakness of one leg which he did not have prior to operation. By taking his tumour out, we have saved him from something worse.

If the tumour is a glioma, we are guided by the type of tumour, its situation, the degree of incapacity which it has already caused, and the further incapacity which may be entailed by removal. Thus a patient with an astrocytoma in the right Rolandic area, who is suffering from severe headache, failure of vision, and occasional epileptic attacks, but with little weakness of his limbs, and little mental impairment—for such a patient we would do a decompression to relieve the pressure symptoms, and would arrange for a course of deep X-ray treatment. To attempt a wide removal of such a tumour would almost certainly produce a hemiplegia, and although it might prolong life for a few months or even longer, the tumour would inevitably recur and cause death. This practice applies to most types of gliomata, although there are some situated on or near the surface of the brain in less eloquent sites where removal, as complete as may be to the naked eye, is justifiable and practicable. With these we usually try to arrange for a course of radiation to deal with the microscopic extensions which we know we have left behind. Thus, we have employed radiotherapy pretty extensively and I should like to take this opportunity of thanking Dr. Jupe, Dr. David Barnes, Dr. Fairchild, and Professor Windeyer among others for their help and co-operation.

In general, we have found that the survival period of treated spongioblastoma multiforme is longer than in the untreated cases, although only the "good cases" are sent for treatment. With the more slowly growing types of gliomata—the astrocytoma and oligodendroglioma—the evidence is very difficult to evaluate, because these tumours behave in such an irregular manner whatever is done to them. Thus it is not very unusual for a patient to present himself with a two or three weeks' history of headache and visual impairment, without any gross neurological abnormalities, and the X-rays reveal a huge area of calcification representing a tumour which must have been present for many months or years without symptoms. A decompression alone may relieve

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It may be a good idea to give a course of treatment as a routine in these cases.

Have we really any evidence that radiation treatment has an effect on brain tumours? I think anyone who has seen the response of a medulloblastoma to a course of X-ray therapy would say yes. But even with these tumours it is a prolongation of life and not a cure which we achieve. Are brain tumours ever cured by radiation? We have experience of one case in which the answer to that, too, is in the affirmative.

In April 1935 a young woman was admitted to the National Hospital, Queen Square, under the care of Dr. Critchley. She had been in good health until two months before admission when, after a mild attack of influenza, she began to complain of progressively severe headache and vomiting, and she had two epileptic attacks characterized by turning of the head and eyes to the left side, and convulsive movements of the left side of the face and left upper limb. After the second of these there was a progressive weakness of the left side of her body. On examination there was bilateral papilloedema, and a slight but definite weakness of the left limbs and face, with a corresponding alteration in the reflexes. X-rays of the skull were normal, but the spinal fluid pressure was elevated and the fluid contained an excess of protein. There was thus little doubt that there was an expanding lesion in the right frontal region, either a rapidly growing glioma or possibly an abscess. At operation Mr. Hugh Cairns found a subcortical glioma in the right frontal lobe. Sufficient of this was removed for histological examination and Dr. Greenfield demonstrated that it was a glioblastoma multiforme, of a malignant type. There was some improvement after operation, notably in the relief of headache and subsidence of papilloedema, but little alteration in the left-sided weakness. Four weeks after operation a course of radium treatment was given, 44,400 mg.-hrs. (100 mg. plaque) directed to the right frontal region.

Improvement continued until January 1936, when she again began to complain of headache, the decompression became very tense, and the left hemiparesis more marked. In the following month, she had a course of high-voltage deep X-ray therapy (200 kV. 1.5 mm. copper filter; 6,600 r in 14 doses; 5 fields, a.p., 2 lateral, superior, vertical), with a rapid improvement in her general health, abatement of the pressure symptoms, and a slight improvement in the neurological abnormalities. In June 1936 there was a rapid worsening of her symptoms: headache, vomiting, drowsiness, and now a complete paralysis of the left arm and nearly complete paralysis of the left leg. She was given a second course of deep therapy (the same physical factors 16 doses, 7,810 r) and again there was a prompt improvement. By October 1936 she had no symptoms, the decompression area was soft and just flush with the skull, the papilloedema had completely subsided, and there was only a slight kinetic weakness of the left hand with a little sensory impairment in this limb. By March 1937 the decompression area was markedly indrawn. She returned to full work in a shop and in June 1939 she was married. She remained well until September 1941, when her left leg suddenly gave way with her when she was coming downstairs. She thought that she had twisted her ankle, but on attempting to rise (there had been no faintness or loss of consciousness) she found that her left arm and leg were completely paralysed. When she was seen on October 4, 1941, she was unable to walk unassisted. The decompression area was still markedly indrawn, and she had no headache or discomfort but there was a profound spastic weakness of the left arm and leg, and to a less extent of the left side of the face. She remained in about this state until February 1942, when she began to have focal epileptic attacks in the left limbs and left side of the face. In March 1942 she was given another course of deep therapy (9,560 r in fifteen days) which had the effect of stopping the focal epilepsy but she gradually deteriorated and died on July 24, 1942, seven and a half years after the onset of symptoms, and six years after the third course of radiation treatment. At the autopsy there was an extensive subcortical necrosis of the right hemisphere, maximal in the irradiated field. Dr. Dorothy Russell could find no relic of the tumour for which the operation had been done and the radiation therapy given. Thus we must assume that the radiation had killed the tumour completely, but in so doing it produced damage to the normal brain which killed the patient.

We believe this necrosis is a radiation effect and not a very uncommon one. We have encountered some 6 or 8 cases of varying degrees of severity, but there are no means of knowing exactly how often it occurs. The effects may not produce clinical manifestations for many months or years after the radiation, and it is probable that in many cases the tumour kills the patient before these effects have had time to develop. Is this a result of overdosage? In none of our cases was the dosage beyond the accepted range of safety, and it should be said that none of them suffered superficial damage (burns or necrosis) to the scalp or skull, except more or less permanent depilation in irradiated fields. However, most of them were treated through multiple portals of entry, so that no one area of the scalp or skull received more than a fraction of the total dose brought to bear on the tumour.

We have not encountered a similar effect in the spinal cord but there are reports in the literature of such effects. Thus Stevenson and Eckhardt have recently described the case of a man who received radiation treatment for lympho-epithelioma of the neck, and who about a year later developed a transverse lesion of the cord at the fourth cervical segment. This led to his death from respiratory paralysis, and at the autopsy there was a necrotic lesion in the cervical enlargement which had much the same appearance as those we have encountered in the brain. It was estimated that the spinal cord had received between 5,000 and 6,000 r of the total treatment given.

Such an effect of radiation makes me more cautious in advising radiation therapy for a lesion which I am not certain can be treated in no other way.

Thus, some years ago, a middle-aged woman came in suffering from peculiar diencephalic attacks and a mild increase in intracranial pressure. A ventriculogram revealed a slight symmetrical hydrocephalus with a filling defect in the posterior part of the third ventricle which we interpreted as the medial extension of a thalamic glioma. She had a decompression done, with great improvement but because of the supposed site and nature of the lesion, she was given X-ray therapy (3,492 r, 1,908 r, 1,440 r) during the next two years. She died three and a half years after her first admission, and at the autopsy there was a massive subcortical necrosis of the right hemisphere, and the only other lesion found was a small colloid cyst in the third ventricle. The right treatment in this case would have been to withhold the X-ray treatment until we had had more information from further ventriculograms when the decompression was no longer adequate.

The possibility of doing damage with our present technique of therapy raises important problems. What is the maximum dose of radiation the brain will tolerate without these necrotic effects? What dose will have the maximum beneficial effect on the tumour and yet not cause necrosis? Should we revise our views about multiple portals of entry and perhaps concentrate on irradiating a tumour exposed at operation?

Dr. Dorothy S. Russell [Summary]: In the histological examination of gliomas which have been treated by deep X-ray therapy it has been impossible, as a rule, to assess the amount of tissue-damage attributable to the treatment owing to the natural occurrence of variable degrees of necrosis, hæmorrhage and vascular changes in untreated tumours.

It is therefore of fundamental importance to gauge the effects of such irradiation upon the normal brain. Two cases of this kind have been mentioned by Mr. Pennybacker. In the first, of which he gave particulars, symptoms proved to be due to a small colloid cyst of the third ventricle. Irradiation necrosis developed beneath a right temporal decompression. In the second case, in a middle-aged man, symptoms referable to a lesion in the left temporal lobe followed nine months after a single dose of 2,350 r had been given for a rodent ulcer of the overlying scalp.

The *macroscopic* appearances in both cases were similar: there was massive necrosis of the subcortical white matter accompanied by numerous small hæmorrhages, and the overlying cortex was broadened and abnormally tough, especially over the summits of the convolutions. *Microscopically*, the subcortical white matter was completely destroyed through a large part of the lobe by necrosis and hæmorrhage, and the necrosis extended in places into the cortex. The latter showed considerable loss of neurones, complete in places, accompanied by a pronounced gliosis. Many of the perforating blood-vessels had undergone fibrinoid necrosis and were often thrombosed, while others showed great collagenous thickening of their walls. In the meninges there was a trivial degree of fibrous thickening and sparse lymphocytic infiltration. Remarkable features were the diffuse permeation of both grey and white matter by numerous threads of fibrin, and the absence of cortical atrophy in spite of the considerable destruction of the neurones.

Animal experiments.—Dr. C. M. Wilson (Physics Department, Westminster Hospital Medical School) has participated in an attempt to find out in what order these changes take place in the brain, and the part played by alterations in blood-vessels. To this end the left side of the skull in a series of 8 rabbits was irradiated with a single dose of 2,850 r. The animals remained perfectly well until about a hundred days later when neurological disturbances developed (3 animals). One of these, kept alive for a further forty days, became blind and unable to feed itself. These three animals showed cerebral lesions similar to those described in the human cases. The foci of necrosis, however, occupied central parts of the brain and were rarely accompanied by demonstrable vascular changes. The cortex immediately below the site of irradiation appeared relatively insusceptible. The left lobe of the cerebellum showed marked changes in both cortex and white matter in two animals.

The remaining 5 rabbits were killed at earlier stages (seventy-three to ninety days after irradiation), before the onset of symptoms, in order to identify early stages of the lesion. In 2 (at eighty-three and ninety days respectively) such changes were observed. They occupied the cerebellum and hippocampus and consisted of minute hæmorrhages. Necrosis of tissue and early focal gliosis were sometimes associated, but no histological alterations were observed in the blood-vessels. It is therefore difficult to attribute the necrosis and hæmorrhage to vascular damage, as appeared likely in the human material. The investigations are being continued, and will be reported later in full. In conclusion the following questions require an answer: What is the significance of the prolonged latent period before the lesions develop? Why are the lesions progressive when they are once initiated? And why, in the experimental animals, are the lesions deep-seated in the cerebrum and not superficial? The answers may be found by the physicist; they appear at present to be insoluble to the pathologist.

Mr. J. Jackson Richmond: There are three problems related to this interesting subject which I would like to discuss briefly. First, the difficulty in selection of cases for irradiation treatment. Dr. McWhirter has stressed the importance of a histological classification in deciding the question. However, very often one meets with surprises. For instance, it is generally stated that the astrocytoma is a radio-resistant tumour, but this is only true when considered as a group. Occasionally these gliomas prove to be relatively radiosensitive. Again it is difficult to assess suitability according to the patient's general clinical condition. Sometimes palliation of years standing follows treatment of patients seemingly in dire straits. This occurs usually but not always with classically radiosensitive tumours, e.g. spongioblastomata or medulloblastomata. Therefore in the light of present knowledge, I accept for treatment a great majority of the cases referred by neurosurgeons unless, of course, the patient is *in extremis*.

Secondly, "Is it worth while giving a second course of irradiation treatment in the case of recurrence following previous radiotherapy?" For the great majority of these cases the answer is "no" but very occasionally it is a justifiable procedure. Although many features of the case will influence the decision, I consider that the most important single factor is the interval of clinical freedom from active disease following the original treatment. If this period is three years or more and the tumour dosage given in the first instance was conservative, then further treatment may arrest the progress of the disease for an appreciable time.

The third point is the importance of irradiating a sufficiently extensive zone of brain tissue to ensure bringing the entire growth to full dosage level. In many cases, clinical localization of the tumour even with the aid of ventriculographic studies can only be approximate. Very often, after surgical exploration, it is impossible to delimit the extent of an invasive tumour. With this in mind it is possible to establish a series of standard regional irradiation techniques which can be modified when necessary to suit individual cases.

Slides were shown illustrating "X-ray field systems" and dosage contours to conform to the above principle. Also an apparatus recently adopted in the treatment of cerebral tumours was briefly described. This was designed to set up a predetermined field of uniform irradiation and at the same time ensure maintenance of beam direction.

Dr. Frank Ellis: I should like to thank the opening speakers for their admirable papers. One point which must be appreciated by all dealing with cerebral tumours is that histological evidence is essential to decide on, and learn from, the treatment given. I should like to ask Dr. McWhirter whether he can be sure that the cases he did not treat with radiation were not radiosensitive, even if his judgment regarding the cases he did treat was considered justified by results. I think that for the present, more evidence is necessary, and that his non-sensitive groups should be treated until the evidence is irrefutable.

Comparatively recently normal nervous tissue was considered insensitive to radiation. In 1934, following treatment for carcinoma of the œsophagus with one of the fields centred over the spinal cord, a patient of mine developed a transient paraplegia. Thinking this might be due to the radiation I consulted the literature and found it teeming with evidence of the damage which can be done by radiation to normal nervous tissue. Most of the histological appearances seemed to consist of focal necroses but they seemed to depend for their nature on the dose and the time after treatment at which the examination was made as well as the age of the animal. Functional changes were also described, especially from Pavlov's Institute by Nemenow, using the disturbance of conditioned reflexes as a criterion. Dr. Russell's experiments showing the increased permeability of the capillaries to a dye soon after radiation are in accord with the accepted view of the effect of radiation. It is an indication that the efficiency of nervous tissue might be seriously influenced by radiation because the resulting disturbance of nutrition might have serious effects. As a student of physiology, I was, for instance, much impressed by the sensitivity of the brain to oxygen lack. The idea has occurred to me that the recurrence of symptoms following treatment might be due to such changes as those described by Dr. Russell occurring, as might be expected, in the region of the tumour. In 7 cases out of 50 treated in the last two-and-a-half years there seems to be reasonable evidence of this. In such cases, further treatment might possibly increase the damage rather than be good for the patient. The doses given have been rather small than otherwise (3,500 to 4,000 r in about three to four weeks). The region treated was usually about 2 cm. beyond the supposed limits of the tumour as indicated by the neurological surgeon. It might be that the extensive necrosis reported by Mr. Pennybacker in his cases was associated with the very high dosage and the frequent treatments.

The immediate effects of radiation in causing improvement when this occurs, might conceivably be due to an inhibition of the secreting activity of the chorionic epithelioma.

Mr. J. E. A. O'Connell: I have been interested in the effects of X-radiation upon the tissues of the central nervous system and was fortunate in having the opportunity of working on this subject in Dr. Percival Bailey's laboratory in Chicago. The results of this investigation were published (O'Connell and Brunschwig, *Brain*, 1937, 60, 230). It has been suggested that the changes in the nervous tissues may be secondary to vascular changes produced by irradiation. The histological changes observed in our investigation were less severe than those mentioned by Dr. Dorothy Russell, but were otherwise of very similar type. In the brains which we examined the evidence of damage to the blood-vessels was slight—an excessive quantity of fat in the walls of the capillary blood-vessels being the only common one. We were therefore led to the conclusion that both the vascular and the nervous damage resulted directly from irradiation and that the latter was not secondary to the former. Secondly, one speaker has suggested that it might be beneficial if brain tumours were irradiated at the time of the operation with the bone flap reflected from the surface of the tumour. This procedure has been carried out in the United States—but not, as far as I know, with benefit. Since it seems likely that the intensity of irradiation is as important a factor as total dosage in producing damage in normal tissues such irradiation at the time of operation might well be unwise on theoretical grounds.

Section of Dermatology

President—SYDNEY THOMSON, M.D.

[April 18, 1946]

Folliculitis Decalvans.—H. CORSI, F.R.C.S.

Male, aged 40.

This patient shows extensive ordinary baldness. In addition, there is, at the sides and back of the scalp, marked loss of hair. The loss of hair is of the parvi-maculata design, somewhat similar to that seen in Brocq's pseudopelade. The whole area, however, shows considerable erythema, and only a few weeks ago many of the follicles were pustular. The beard area and moustache area are normal.

The patient was given Fowler's solution \frac{mii} three times a day, for two months, and it was during and subsequent to this that the acute activity in the follicles ceased.

A Wassermann test was negative.

On the whole the case appears to be the type of folliculitis decalvans described by Quinquaud, but the even distribution of the bald patches is atypical, and there is possibly an alternative diagnosis which could be suggested.

POSTSCRIPT.—Subsequent examinations for favus or other fungus proved negative.

Dr. F. F. Hellier: I have seen recently a case of scarring alopecia which was due, as far as I could make out, to tropical lichenoid dermatitis. The man had lichen-planus-like lesions on his body, face, and scalp. He had been taking mepacrine and had been in West Africa. Has any member seen one of these cases of scarring alopecia and watched it right through to a finish? I have not done so myself and I should like to know the prognosis.

Dr. G. B. Mitchell-Heggs: I have under my care a student with folliculitis, loss of hair and scarring, involving the scalp and eyebrow. Bacteriological examination of the hair follicles revealed a staphylococcus, resistant to penicillin, but sensitive to sulphathiazole. The latter was prescribed, and the condition has improved. It is perhaps early to discuss cure, as only three months have elapsed. Except for involvement of eyebrow, it is similar to Dr. Corsi's case.

? **Acne Conglobata.**—H. J. WALLACE, M.D.

Miss G. C., aged 30, Secretary.

The patient has noticed small nodules in various parts of the body for the past thirteen years some of which grow for a time and then disappear; others she thinks have been persistent. They first appeared in the right axilla thirteen years ago. They usually grow for about six weeks and then burst, discharging yellowish pus. Most other parts of the body have been affected from time to time. Recently the lesions have been most prominent in the peri-anal area, and it was for a series of sinuses, resulting from discharging nodules, in this area, that she sought advice. She is at present under the care of Mr. Boggon at St. Thomas's Hospital. One nodule with sinus was excised, with the following pathological report:

"Sections show a filterless tract in the subcutaneous tissue and communicating with the surface. There is an acute and subacute inflammatory reaction with polymorphs, plasma cells and fibroblasts numerous. Gram-stained section shows a number of Gram-positive globoid bodies resembling monilia (yeasts). No cocci seen. The inflammatory reaction extends for some distance into the surrounding tissue."

Pus from one of these lesions showed *Staphylococcus aureus*. Another nodule has been excised; histology was typical of a sebaceous cyst.

On examination.—Nodules with much scarring, together with sinus formation, can be seen especially in the buttock, together with other typical nodules in the skin, particularly on the trunk.

Comment.—This condition is well marked in the patient's family. She has five brothers and four sisters, of whom two brothers and two sisters are afflicted but in lesser degree, and in some the process seems to have died out.

Dr. F. Parkes Weber: There can be no doubt that this interesting case is one of what has been termed "sebocystomatosis" or "steatocystoma multiplex". I do not see why one should not call it by the third or common name, "hereditary sebaceous cysts", though the sebaceous cysts are not limited to the scalp. The dominant Mendelian heredity and the great number of relatives affected are typical.

In the present patient some of the sebaceous cysts have become secondarily infected with pyogenic organisms and the resulting suppuration has been associated with a tendency to sinus formation.

A most interesting feature in this particular case, is its association, mostly in the spring, with what can be called recurrent suppurative hidro-adenitis axillaris, which is well known and not rare. The association may, however, be a chance one. I am not sure whether there is any connexion between the sweat gland disease and the hereditary sebaceous cysts.

The complication of the suppurating sinuses in the fat region of the buttocks is a very disagreeable feature of the case.

Dr. F. F. Hellier: There are one or two points which I might recall concerning a case I described in 1939 (*Brit. J. Derm.* (1939), 51, 109). The man had a severe acne over his whole back, right down on to the buttocks, with tunnelling and sinus formation, and characteristic bridge-scars. The diagnosis was not in doubt. He had many cysts and, in reference to what Dr. Parkes Weber has said, I am sure that his acne was not due to sebaceous cysts. He had enormous scarring over the whole back and isolated sebaceous cysts. I feel that there were two conditions—the cysts and the acne lesions—running side by side.

When I saw the first of my cases with cysts, I wondered whether they were retention cysts, caused by the scarring. I began to look up the man's family. I found a sister in a local asylum with a lesion like a rhinophyma, exactly like her brother, and a large cyst hanging pendulously from her ear. I felt it unlikely that there could be a retention cyst and scarring on the lobe of the ear, and I considered it was a congenital cystic condition. All the family had a marked degree of what one might describe as *kérose*. I think another member had also been in an asylum and they were all of rather low mentality. This may have been a coincidence; it was obviously running through the family. I feel there was some underlying fault in the germ plasm which had led to a series of defects.

Dr. A. C. Roxburgh: The case seems to me to be much more an infection of the sweat glands than one of a sebaceous nature. It is not in the least like a case of *sebocystomatosis* I saw in 1938. That woman had a large number of cysts over the sternum, anterior axillary folds and round the lower thorax, all of which contained a peculiar oily kind of grease. I should not think this was even a case of *acne conglobata*.

The President: One point about the case is that the woman's back, particularly on the right side, shows some small tumours in the dermis which are not, apparently, connected in any way with the conglobata lesions, but which are rather bluer and more translucent. Those reminded me of *syringomata*.

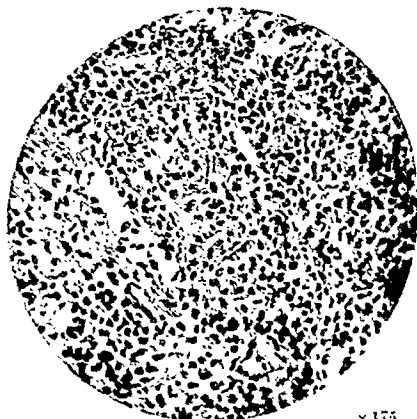
Eosinophilic Granuloma.—C. L. COLLINS, M.B.

Mrs. E. H., aged 38, had noticed a small swelling in the left groin about seven weeks before I saw her in Dr. Duckworth's clinic at St. John's Hospital, a few weeks ago. During the seven weeks the swelling had increased and had become a small tumour, painless, circumscribed, oval, dusky red, and soft.

The tumour was excised and the microscopical findings were as follows: There are foci of reticulum cells in the corium, especially in the upper fourth. These foci are infiltrated with and surrounded by eosinophilic cells.



×35



×175

Eosinophilic granuloma.

The white cell count was: W.B.C. 12,400 per c.mm., of which 68% were polymorphs; 4% eosinophils; 28% lymphocytes; no monocytes seen. This white cell count contrasts with that seen in previous cases, described by A. Pasini (*G. ital. Derm. Sif.*, 1940, 81, 1) and P. Cerutti (*Dermatologica*, 1942, 85, 90), in which there was a morbid eosinophilia, amounting to 40%.

Lichen Sclerosus et Atrophicus (Lichen Planus Morpheicus).—BERNARD GREEN, M.R.C.S., L.R.C.P.

Miss D. B., aged 17 years.

The first lesion commenced about six years ago as a small papule over the right scapula: A few more papules appeared slowly and about eight months ago the condition began

to spread. The lesions now consist of two main plaques situated over the right scapula, composed of irregular, slightly elevated, flat topped, mother-of-pearl papules. In addition to the two main plaques there is a number of discrete papules scattered across the shoulders. Some show a slight depression in the centre; others have a horny comedo-like plug in the centre situated at the pilosebaceous orifices. Atrophy is present as a tissue-paper-like wrinkling, simulating that seen in atrophic forms of morphea. Her general health is good and there is nothing to suggest any endocrine disturbance.

This condition is said to be a distinct entity. It is more common among women and is said to occur more frequently in the later stages of life.

Atrophic forms of lichen planus can simulate this disease, but usually one can find some typical lichen planus papules in some of the lesions. In addition lichen planus is much more rapid in its development. I think, therefore, that the name lichen sclerosus et atrophicus is more suited to this complaint than lichen planus morpheicus.

Histological report.—The epidermis is thinned and covered by a thickened stratum corneum which also extends into the lanugo follicles. The collagen in the superficial layer of the corium is homogeneous and condensed.

Dr. F. Parkes Weber: This is an example for those who would like to believe that lichen sclerosus et atrophicus is a variety of morphea. It may be called "lichen sclerosus et atrophicus", but I suggest that it may justifiably be regarded as what I would term "morpheic scleroderma of the lichen sclerosus et atrophicus type".

The President: I remember one similar case shown many years ago in regard to which Dr. Sibley made the clinical diagnosis. Subsequently a biopsy was done and to everyone else's surprise there was a definite lichen planus histology.

Dr. H. Corsi: So long as we remain in ignorance of the nature of many skin diseases, the terms by which we designate them are mostly mere statements of physical signs. In that group of physical signs which we call lichen planus, the cases are as a rule typical, so that there is no difficulty in diagnosis. If the case is atypical, there will be, in most instances, the unmistakable papule of lichen planus discoverable somewhere; so that even if the major portion of the eruption is horny, or atrophic, or vesicular, it is still recognizable as an example of the disease we call "lichen planus".

In 1915 Sir Ernest Graham-Little began to show a series of cases of atrophic spinulosis of the scalp, without affection in any other part of the body. The subject "syndrome Graham-Little" has been taken up in foreign literature in relation to the pseudopelade described by Brocq. Coincidentally I have come across this literature in reading up the subject of folliculitis decalvans in connexion with the case of atrophic folliculitis of the scalp which I have shown here to-day.

In 1937¹ I showed a case of lichen spinulosis of the scalp, type Graham-Little, at this Section. This patient had lesions typical of lichen planus and also suffered from a vesicular eruption about the nails of hands and feet. The nails fell off and never grew again—another rare manifestation of "lichen planus". I was able to show a similar case a month later, though I have never seen another since. From my two cases, and from certain other cases described in foreign journals,¹ it seems fairly certain that atrophic lichen spinulosis of the scalp, atrophic onychomadesis, perhaps also white-spot disease, and therefore some forms of scleroderma, are all varieties of that disease, which, from its most frequent physical sign, we call "lichen planus".

It seems that "lichen planus" may show almost every physical sign which can be met with in dermatology, and it appears to me that Dr. Green's case of atrophic or sclerotic spinulosis of the skin of the back can very well be an atypical form of lichen planus.

¹ See Bibliography under Corsi: Atrophy of Hair Follicles and Nail-Matrix in Lichen Planus. *Brit. J. Dermat.*, 1937, 49, 376-384.

Linear Nævus Treated by Thorium X.—P. J. FEENY, M.B.

J. R., a girl aged 10 years.

A linear nævus, maximum length $1\frac{1}{2}$ in., maximum width 2 in., was present on the outer surface of the right upper limb. Test areas had been treated by CO₂ snow, sodium morrhuate injection and radium plate; the main mass had then been treated by thorium X, affording an opportunity for comparing their merits in this type of case (i.e. the mixed type). The nævus extended from the middle of the outer surface of the right arm down the outer surface of the forearm and the back of the hand to the nail-fold of the forefinger (the nail being split longitudinally) and ended on the middle finger at the level of the proximal interphalangeal joint. It was first noticed at the age of eighteen months.

Treatment.—CO₂ to marked area on arm when aged 6½ years. A month later had sodium morrhuate injection to another marked area on the arm. At age 8 had 8 mg. radium plate to the marked area at the edge of the lesion halfway down the forearm. This test area showed atrophy and telangiectases.

Ten months ago treatment by thorium X was commenced, 1,500 e.s.u. per c.c. in varnish once a month. For the past three months, the portion on the hand and fingers has been treated fortnightly, last treatment a week ago.

The response was immediate and noticeable after the first treatment. It has been so satisfactory that no further treatment is necessary.

[May 16, 1946]

Lichen Sclerosus.—GODFREY BAMBER, M.D.

T. G., aged 14. The first lesions on this girl's skin appeared two and a half years ago on the front of the left hip and on the back of the right thigh, and a little later on the fronts of the ankles. Later lesions developed near the point of the right elbow, and over the left scapula. These lesions were said to be white and slightly scaly. About six months ago white lines began to show on the outer side of the right arm. The general health has been good.

The appearance of the larger plaques when I first saw her in January last had been altered by treatment with thorium X, but that of some of the smaller lesions was characteristic of lichen sclerosus, a white shiny surface with some scaling and pitting.

The linear lesions on the arm are an unusual feature of this condition. The finest looked nothing more than thin lines of depigmentation, but when some of the wider ones were examined with a lens the surface looked somewhat shiny and a little atrophic. So far no scaling has developed on these linear lesions.

Histology.—A piece was removed from the lesion near the right elbow, and the section confirms the diagnosis.

POSTSCRIPT (21.8.46).—When the patient was seen recently the linear lesions were less apparent.—G. B.

Dr. W. Freudenthal: It would be worth while to examine these fine streaks histologically.

Dr. F. Parkes Weber: I think that one ought to call these cases "morphœic sclerodermia of the lichen sclerosus et atrophicus type". I think these cases represent a variety of morphœic sclerodermia and that "lichen sclerosus et atrophicus" is a more recent term which should not be allowed to displace the older and more inclusive term, "morphœic sclerodermia".

Dr. A. C. Roxburgh (chairman): The question seems to be whether lichen sclerosus is essentially an atrophic lichen planus or a scleroderma. The evidence seems to be accumulating that it is more of a scleroderma than a lichen planus.

Calcinosis Circumscripta.—GEOFFREY DUCKWORTH, M.R.C.P., and M. GROSSMANN, M.D.

Mrs. M. C., aged 50. Since March 1945 has complained of swollen and painful finger tips; lassitude; "rheumatism" in the knees; and indigestion occasionally. For fifteen years the fingers have exhibited Raynaud's phenomenon when exposed to cold, even of a mild degree.

On examination.—The tips of the fingers are seen to be enlarged, and shining through the epidermis are irregularly shaped whitish macules of a fairly hard consistency. These are present also on the inner side of the little finger of the left hand. They are made much more prominent by squeezing the adjoining tissues. On the right knee, in front, is a red patch of chronic eczema. There are no signs of scleroderma, or dysphagia.

One of these painful white nodules ulcerated through the skin. Another was excised and found to consist of lime salts (the carbonate and phosphate of calcium). A biopsy revealed a curious picture—deep in the cutis was an epidermoid cyst of the implantation type, extending to the surface (fig. 1). Unfortunately it was empty when examined

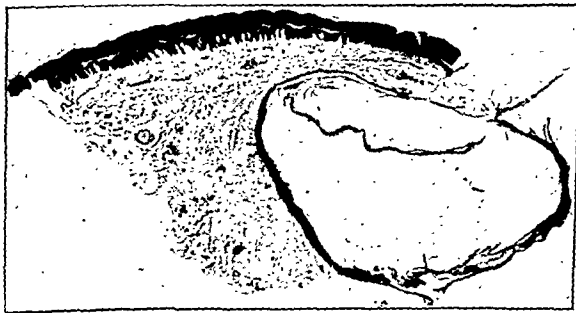


FIG. 1.—Calcinosis circumscripta. Section showing the curious cyst with its epidermal lining, deep in the corium. $\times 5$.

microscopically. A blood-count showed: R.B.C. 4.75 millions per c.mm.; Hb. 95%; C.I. 1.0. Total W.B.C. 4,550 per c.mm. **Differential:** Polys. 59%, lymphos. 29%, monos. 9%, eosinos. 3%, basos. nil. No abnormal types of cells were seen. The blood calcium was 11.1 mg. per 100 c.c.; phosphorus 4.5; and uric acid 3.5. The W.R. was negative.

Her past medical history was uneventful. Menopause six years ago.

The X-ray appearances are typical of calcinosis circumscripta. The other parts of the skeleton show no evidence of any abnormal calcification, in particular the elbows and knees where such calcifications are described in the condition of scleroderma and Raynaud's disease.

Why such a condition should occur is not known, but there is an interesting account of the pathogenesis in a paper, Cutaneous and Subcutaneous Calcinosis, by F. R. B. Atkinson and F. Parkes Weber (1938) *Brit. J. Derm.*, 50, 267.

Dr. M. Grossmann: The X-ray appearances of Dr. Duckworth's case are typical of calcinosis circumscripta (hypodermololithiasis, Kalkgicht).

There are dense granular opacities in the soft tissue shadows, chiefly of the terminal phalanges, surrounding the tufts (lateral views show that the opacities are situated on the flexor aspect).

Similar small nodular opacities are present at the radial aspect of the middle phalanges of the right index and middle finger (fig. 2).

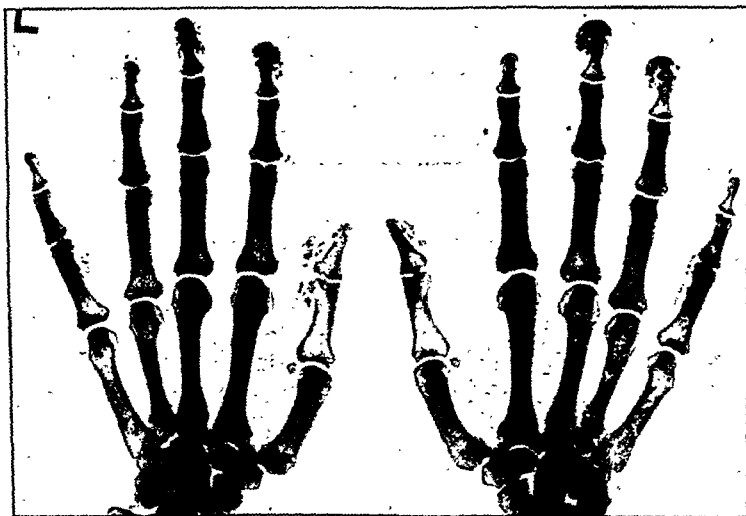


FIG. 2.

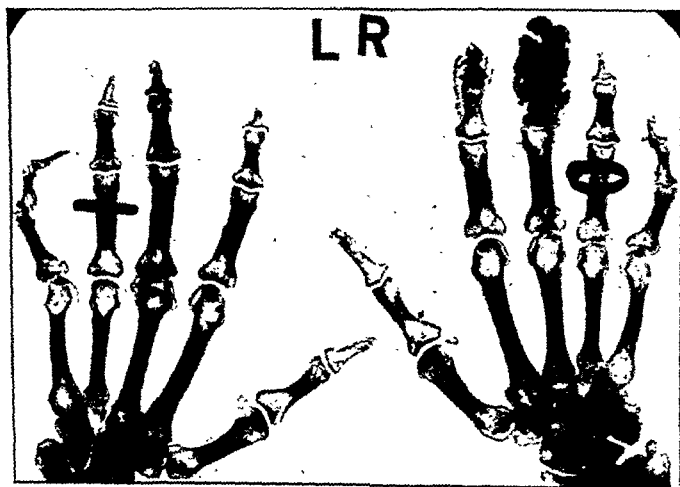


FIG. 3.

A linear, partly lobulated calcium deposit is shown at the radial aspect of the right little finger and irregular calcifications at the radial aspect of the middle phalanx of the left index and the proximal phalanx of the left little finger.

The soft tissue shadows of the hands show no other abnormality of note.

The metacarpophalangeal and interphalangeal joints show very slight lipping of the joint surfaces, suggesting early osteo-arthritic changes.

There is no other bony abnormality noted, in particular no evidence of absorption of the cancellous tuft of the phalanges nor any osteoporosis.

These radiological appearances may be produced by: Thrombo-angiitis obliterans, Raynaud's disease, scleroderma, sclerodactylia.

[May 16, 1946]

Lichen Sclerosus.—GODFREY BAMBER, M.D.

T. G., aged 14. The first lesions on this girl's skin appeared two and a half years ago on the front of the left hip and on the back of the right thigh, and a little later on the fronts of the ankles. Later lesions developed near the point of the right elbow, and over the left scapula. These lesions were said to be white and slightly scaly. About six months ago white lines began to show on the outer side of the right arm. The general health has been good.

The appearance of the larger plaques when I first saw her in January last had been altered by treatment with thorium X, but that of some of the smaller lesions was characteristic of lichen sclerosus, a white shiny surface with some scaling and pitting.

The linear lesions on the arm are an unusual feature of this condition. The finest looked nothing more than thin lines of depigmentation, but when some of the wider ones were examined with a lens the surface looked somewhat shiny and a little atrophic. So far no scaling has developed on these linear lesions.

Histology.—A piece was removed from the lesion near the right elbow, and the section confirms the diagnosis.

Postscript (21.8.46).—When the patient was seen recently the linear lesions were less apparent.—G. B.

Dr. W. Freudenthal: It would be worth while to examine these fine streaks histologically.

Dr. F. Parkes Weber: I think that one ought to call these cases "morphœic sclerodermia of the lichen sclerosus et atrophicus type". I think these cases represent a variety of morphœic sclerodermia and that "lichen sclerosus et atrophicus" is a more recent term which should not be allowed to displace the older and more inclusive term, "morphœic sclerodermia".

Dr. A. C. Roxburgh (chairman): The question seems to be whether lichen sclerosus is essentially an atrophic lichen planus or a scleroderma. The evidence seems to be accumulating that it is more of a scleroderma than a lichen planus.

Calcinosis Circumscripta.—GEOFFREY DUCKWORTH, M.R.C.P., and M. GROSSMANN, M.D.

Mrs. M. C., aged 50. Since March 1945 has complained of swollen and painful finger tips; lassitude; "rheumatism" in the knees; and indigestion occasionally. For fifteen years the fingers have exhibited Raynaud's phenomenon when exposed to cold, even of a mild degree.

On examination.—The tips of the fingers are seen to be enlarged, and shining through the epidermis are irregularly shaped whitish macules of a fairly hard consistency. These are present also on the inner side of the little finger of the left hand. They are made much more prominent by squeezing the adjoining tissues. On the right knee, in front, is a red patch of chronic eczema. There are no signs of scleroderma, or dysphagia.

One of these painful white nodules ulcerated through the skin. Another was excised and found to consist of lime salts (the carbonate and phosphate of calcium). A biopsy revealed a curious picture—deep in the cutis was an epidermoid cyst of the implantation type, extending to the surface (fig. 1). Unfortunately it was empty when examined

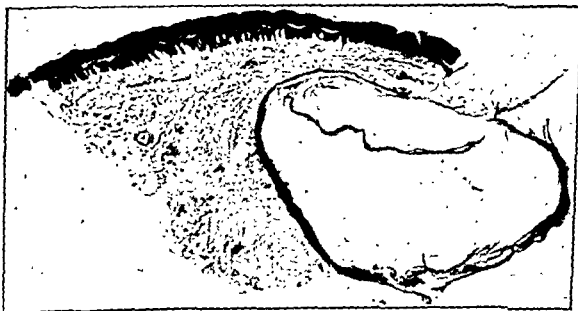


FIG. 1.—Calcinosis circumscripta. Section showing the curious cyst with its epidermal lining, deep in the corium. $\times 5$.

microscopically. A blood-count showed: R.B.C. 4.75 millions per c.mm.; Hb. 95%; C.I. 1.0. Total W.B.C. 4,550 per c.mm. **Differential:** Polys. 59%, lymphos. 29%, monos. 9%, eosinos. 3%, basos. nil. No abnormal types of cells were seen. The blood calcium was 11.1 mg. per 100 c.c.; phosphorus 4.5; and uric acid 3.5. The W.R. was negative.

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which was sensitive to sulphathiazole but quite insensitive to penicillin. The hairs and scalp were examined for favus, but this was negative. He was given a course of sulphathiazole four-hourly for seven days, and from that time until a month or two ago he had used simple sulphur ointment, which brought about improvement, and up to the present time he had had no further extension and no further hair loss. I might add that last weekend he spent two days sun-bathing, following which he got a dermatitis on his face and neck which has since subsided. It was thought that that was due to photo-sensitivity from his sulphonamide.

Bowen's Disease associated with Anaplastic Carcinomatous Tumour.—G. B. MITCHELL-HECCS, F.R.C.P., and K. D. CROW, M.B.

Woman, aged 57. In 1936 she developed an irritating rash, so-called, on the inner aspect of the left thigh, and this gradually extended until in 1942 a lump developed in the centre of it. As far as we can gather, the lesion was composed, in the first place, of rather small nodules. About this time she had a lot of crusting, and the crusts when removed showed oozing and bleeding underneath. She was admitted to hospital in 1945 and the tumour was excised from the centre of the lesion and an inguinal lymph gland which was enlarged was also removed. The biopsy from the tumour in the middle of the lesion and the lymph gland both showed anaplastic squamous carcinoma. Her Wassermann reaction was negative, and there was nothing relevant in her previous history. This case has been shown for views on the most suitable treatment, but the treatment which has been contemplated is a wide excision followed by skin-grafting.

Histology.—(Professor W. D. Newcomb): Many large and irregular cells, some undergoing mitotic division in the epidermis. Many lymphocytes in papillary layer of dermis.

The Chairman: Is it usual for Bowen's disease to show these oozing surfaces? Are there any suggestions for treatment? How do these cases respond to radiotherapy? If I had one myself I would prefer surgical excision.

Dr. A. N. P. Milner: These cases are supposed not to respond to radiotherapy. Recently a case was sent to me which had failed to respond to treatment by a radiologist.

Two Cases of Folliculitis Varioliformis and Dermatitis Papillaris Capilliti.—A. N. P. MILNER, M.D.

I have shown these two cases to draw attention to certain similarities which suggest that they are not separate entities. They and also the condition known as perifolliculitis abscedens et suffodiens may, I think, be regarded as complications of a primary destructive folliculitis typified in its mildest form by folliculitis varioliformis.

Both cases suffered from acne vulgaris for some years prior to the onset of the scalp condition and, in each case, after development of the scalp condition, the acne vulgaris became quiescent. Both exhibit cribriform scars and indurated nodules; in the former case, pitted scars and, in the latter, nodules predominate. The early lesions of both conditions consist of brownish-red papules pierced by hairs which develop into sluggish pustules capped by scales. Perifollicular spread is common to both and demonstrated by confluent pitted scars in the former and by hypertrophic fibromatous nodules and inter-connecting bridges in the latter.

The section from the case of dermatitis papillaris capilliti displays marked folliculitis and perifolliculitis with a deep-seated fibromatous reaction in the corium.

Seborrhœic Sycosis.—A. N. P. MILNER, M.D.

I have shown this case in antithesis to the other two. Seborrhœic sycosis does not form follicular scars on healing and does not occur apart from seborrhœic dermatitis or a history of a recent attack of this disease. The inflammatory process is largely perifollicular and not destructive of the hair follicles. The infecting agents, staphylococci, are the same in both seborrhœic sycosis and destructive folliculitis of the scalp. The seborrhœic factors seem to protect the follicles in some way not understood. The alopecia pityroides, so called, often found in association with acne vulgaris and seborrhœic conditions, is more probably due to endocrine disorder brought about by overactivity of the sex glands and will usually respond to stilbœstrol. The seborrhœic condition is probably coincidental rather than causative in this form of alopecia.

Dr. C. H. Whittle: I showed a case in an Italian prisoner of war a year ago which I think would probably be classified as a cicatricial sycosis. The appearance in the hair margin was very similar to that seen in one of Dr. Milner's cases. It had resisted all forms of treatment for years, but one of the members at the meeting suggested penicillin locally, and this was tried. The patient, who lives at a distance, writes gratefully to say that the local application of penicillin cream clears up the condition quickly, but it does not remain clear for very long without further treatment.

Some authors have observed similar deposits in lupus vulgaris and erythematodes. Other sites should be examined as similar opacities may be present about the elbows and knees.

Dr. Grossmann showed slides of a case where calcareous deposits were found in the hands of a woman, aged 56, suffering from syringomyelia. This patient developed Morvan's disease of the right hand; in 1941 a whitlow of the tip of the right middle finger was opened and chalky material removed (fig. 3).

In March 1946 the patient attended again for a recurrence of the swelling of the finger.

The radiograph of her hands shows some osteoporosis of the joints with osteo-arthritic changes, but no radiological evidence of such changes as are commonly observed in neuropathic joint lesions with disorganization of the articular surfaces. There is, however, an osteolytic process of the tufts of the terminal phalanges of the left index and ring finger and the right index and little finger giving them a short and pointed appearance caused by partial absorption commencing distally. Extensive calcification is present in the palmar aspect of the terminal phalanges of most of the fingers of the right hand and of the proximal phalanx of the thumb. The distal interphalangeal joints of the left thumb, index and middle finger and the tip of the left little finger show minute calcified deposits.

Calcification in neuropathic joints may appear near the affected joints but is rarely seen in the tip of the phalanges.

Dr. F. Parkes Weber: Some of the earlier cases of cutaneous and subcutaneous calcinosis were published by myself, with or without other doctors. Dr. Duckworth's and Dr. Grossmann's cases are to my mind examples of calcinosis in the fingers occurring in individuals with Raynaud-like symptoms in the hands—i.e. patients subject to "dead fingers." Both patients (including the one with syringomyelia) have had recurrent Raynaud-like symptoms. The commonest type of calcinosis in the fingers is that associated with the sclerodactylia type of scleroderma, which is nearly always accompanied (at some stage) by Raynaud-like symptoms. The rare cases of Drs. Duckworth and Grossmann help to illustrate the whole subject of finger-calcinosis.

Dr. H. D. Haldin-Davis: I should like to know whether there was any calcinosis around the olecranon. About thirty-five years ago I had a case of a youngish woman with calcification of the fingers and around the olecranon. That case was also seen by Dr. Parkes Weber. She died not long afterwards, although apparently a healthy woman at the time I saw her.

Dr. F. Parkes Weber: I have no doubt that I could find amongst my notes and cuttings the case to which Dr. Haldin-Davis has alluded, but I have got a large collection. Perhaps I may be allowed to add a word about the so-called dermoid cyst in the finger. I cannot admit that it is a dermoid cyst in the ordinary sense of the term. I should explain it as a necrobiotic change accompanying and preceding the calcareous deposition. Without that change the calcareous deposit would not be present. The necrobiotic change permits the deposition of calcium salts. After a time the necrobiotic tissue becomes actually necrotic, not merely necrobiotic, and as a foreign body becomes surrounded by a fibrous capsule. Ultimately the calcareous material may be extruded like a foreign body or the uratic contents of a gouty tophus.

Telangiectasia Macularis Eruptiva Perstans.—G. B. MITCHELL-HEGGS, F.R.C.P., and K. D. CROW, M.B.

Man, aged 47, clerical worker. His condition commenced in 1928, when he noticed an eruption of purpuric-like lesions around the ankles. These faded and left persistent brownish-red stains, involving later his legs, thighs, abdomen and a few on the arms. Fresh lesions had erupted and the patient thought that at different times some of the older lesions became redder. He had a severe gum infection.

He was seen by Dr. Mitchell-Heggs in February 1946 and it was then considered that the essential lesion was a telangiectasia rather than a pupura. He did not take any drugs. He had had pulmonary tuberculosis, but had had no gold therapy for it. There was no family history of telangiectasia or other hæmorrhagic disease. When first seen he had a generalized eruption consisting of telangiectatic areas and other orange-red or even brownish macules about 1 or 2 mm. across. At no time was urtication demonstrated, and the blood-count was normal, as were the clotting and bleeding times. A biopsy showed perivascular infiltration in the upper part of the corium.

Dr. F. Parkes Weber: As regards the diagnosis, I agree that this is a case of what I thought ought to be called "telangiectasia macularis eruptiva perstans," but it is a very rare type. The ordinary cases are in very fat, florid women, and the symptoms appear rather later in life than in this man. Osler, however, published a case in a male which was probably of this kind, but under quite a different name. Anyhow, there are rare cases in men, probably commencing at a younger age than those typical ones in women. I would like to emphasize the complete absence of urtication in the present case and I am looking forward, of course, to the biopsy report in regard to tissue mast-cells in the lesions.

Folliculitis Decalvans associated with Penicillin-resistant *Staph. aureus* Infection.—G. B. MITCHELL-HEGGS, F.R.C.P., and K. D. CROW, M.B.

In 1943 a medical student aged 23 came to see Dr. Mitchell-Heggs complaining of increasing baldness. He had thin wiry hair, and there were areas where the hair was completely absent. He also had diffuse thin eyebrows. On examination of the hair it was found that deeper down in the follicle there was in fact pus. The hairs were fairly formed, but bacteriological examination showed a pure growth of *Staph. aureus*

which was sensitive to sulphathiazole but quite insensitive to penicillin. The hairs and scalp were examined for favus, but this was negative. He was given a course of sulphathiazole four-hourly for seven days, and from that time until a month or two ago he had used simple sulphur ointment, which brought about improvement, and up to the present time he had had no further extension and no further hair loss. I might add that last weekend he spent two days sun-bathing, following which he got a dermatitis on his face and neck which has since subsided. It was thought that that was due to photo-sensitivity from his sulphonamide.

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Parapsoriasis.—BRIAN RUSSELL, M.D.

A married woman, aged 39, with a non-irritating rash on the calves and forearms which began in the summer of 1944, later spreading to the arms and thighs. She attributed it to emotional disturbances in connexion with flying bombs. On examination, the almost confluent, slightly scaly discs on all limbs, some showing depressed yellow adherent scales, do not give any bleeding points on scraping. There is no family history of psoriasis and the blood Wassermann and Kahn reactions are negative. The lesions improved very slightly with ultraviolet light therapy. The diagnosis of parapsoriasis is made because of: (1) Complete lack of irritation; (2) the presence of scaly, somewhat psoriasiform lesions but without bleeding points on scraping; (3) a distribution not typical of psoriasis; (4) lack of involvement of the nails and scalp; and (5) the intractability of the condition which has responded little, if at all, to ultraviolet light or other treatment.

The patient is anxious about her condition and suggestions as to treatment would be welcome.

Dr. Parkes Weber: This case is one of "parapsoriasis" as a symptom-term, in the sense that the clinical appearance is somewhat like psoriasis. I suggest that in this patient the condition is really one of true psoriasis, though symptomatically somewhat atypical, and that treatment should be carried out in accordance with this view.

Lichen Planus Atrophicus.—BRIAN RUSSELL, M.D.

The patient is a soldier, aged 25, with an irritating circular lesion on his right breast of ten months' duration which previously had been treated with iodine. On first examination of the polycyclic depressed bluish area, with comedo-like plugs in several follicles and with a pink, slightly scaly, raised edge, tinea circinata was excluded microscopically and a tentative diagnosis of erythema annulare centrifugum or of érythème fixé was made. There was, however, no history of ingestion of phenolphthaleïn or other drugs liable to produce the latter eruption. On his second attendance a solitary papule of lichen planus was found on the front of the wrist. The patient also now shows annular lesions on the left shoulder and on the penis, without pigmentary changes on the latter. Mucosæ are normal. The Wassermann and Kahn reactions are negative. The section supports the diagnosis of lichen planus atrophicus et annulare, revealing hyperkeratosis, thin short rete-pegs, acanthosis, some separation of the epidermis from the dermis, and fibrotic changes round the skin appendages.

Dr. Parkes Weber: I think the case should be termed one of lichen planus annularis atrophicus, and that one should not omit the word "annularis". The lesion on the penis is absolutely typical, and the site is a common one. The tendencies are I think for the disease to get better any way after a time, especially if the mental condition is satisfactory.

Parapsoriasis—Lichenoid Type.—C. H. WHITTLE, M.D.

A. E. E., aged 54, Dairy farmer. Twelve weeks' history of a papular eruption on the wrists, which spread over the arms, trunk and legs. The onset coincided with an attack of bronchitis, which was preceded by a sore throat.

Family history and previous history, *nil ad rem*.

The eruption consists of bluish-red to brownish-red papules, from a millimetre to 2 centimetres in diameter, with frequently shiny tops and milk-white striæ, resembling lichen planus. They do not itch, however, and there are none to be seen on the mucosæ. They are thickly set on the forearms and thighs and less thickly on the trunk. The larger lesions, chiefly on the trunk, have become complete rings, raised bluish-red with a flat, fawn-coloured centre.

There is a collection of papules on his right shin where the skin is congested and thick and which followed a graze a week or so before the lesions appeared on the wrists. There are some fine delicate rings on the penis. There is no glandular enlargement detectable and he feels well. Wassermann negative.

Every effort will be made to follow the subsequent history of this case.

The lesions have been present for twelve weeks and it is early to say what they are going to do at this stage. Their annular lichen planus-like appearance has persuaded most members to regard the case as lichen planus, in spite of certain points slightly against that diagnosis.

Dr. Brian Russell: I think Dr. Whittle's case might be lichen planus.

The Chairman: I certainly thought it was an annular lichen planus.

POSTSCRIPT (30.8.46).—He states that the eruption has now almost disappeared, there being only a few spots left on the hips, and no fresh spots have appeared. The treatment given was liq. arsenicalis minimis 5 to 8 t.d.s. for three months. The diagnosis of lichen planus is the more likely.—C. H. W.

R. G. Cochrane, M.D., F.R.C.P., read a paper on: **The Significant Cellular Changes in the Corium in the Pathology and Diagnosis of Leprosy.**

Section for the Study of Disease in Children

President—Professor NORMAN B. CAPON, M.D.

[April 26, 1946]

Multiple Achalasia, Vertebral Defects and Retarded Growth.—JOHN APLEY, M.D., M.R.C.P.
(by permission of Professor C. BRUCE PERRY).

F. C., at the age of 6, is a puny edition of his normal younger brother, who is only 3 years old (fig. 1).

There are four salient features in the history, and with each a physical abnormality is associated. Their significance can best be emphasized by considering each of these aspects in turn.

(i) *Development.*—There was some delay in passing the customary milestones of physical development. Now, at the age of 6, though the head is the anticipated size for age, the boy is 4 to 5 in. shorter than the average and is of slight build. His proportions are not, however, typically infantile; as an instance, the height is exceeded by the arm span. X-ray of the wrists indicates that skeletal development is barely within the lowest limit of normality.

Mentally bright, I.Q. normal. Psychiatric examination also shows no significant deviation.

(ii) *Enuresis.*—He has always been incontinent and precipitate of urine. Six months ago he came up to hospital with a bladder distended to the umbilicus, and suffering from overflow incontinence. After spinal anaesthesia up to the level of the fifth dorsal vertebra, the distension slowly receded, but the original incontinence and precipitancy were not appreciably relieved. He passes an average amount of normal urine. Intravenous pyelograph normal. Mr. Wilfrid Adams considered the dysfunction was in the nature of an achalasia.

(iii) *Encopresis.*—Though the patient has always been constipated, he has no control over defaecation. He suffers from attacks of abdominal pain and distension, and at these times the constipation is extremely marked. *Barium enema.*—Typical megacolon, with dilatation extending down to the anal sphincter. Unfortunately the spinal anaesthetic had no effect on the lower bowel symptoms.

(iv) *Vomiting.*—Occasional vomiting soon after eating, and not associated with discomfort or malaise. At the age of 3 he vomited after every meal for several weeks. Furthermore, he seems unable to eat more than a small amount at any meal. *Barium swallow.*—Stomach and duodenum normal but oesophagus enlarged.

Thus, four abnormal findings were directly suggested by the history. In addition, there is a dimple in the skin over the lower sacrum, and a tuft of hair over the upper

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A. E. E., aged 54, Dairy farmer. Twelve weeks' history of a papular eruption on the wrists, which spread over the arms, trunk and legs. The onset coincided with an attack of bronchitis, which was preceded by a sore throat.

Family history and previous history, *nil ad rem*.

The eruption consists of bluish-red to brownish-red papules, from a millimetre to 2 centimetres in diameter, with frequently shiny tops and milk-white striae, resembling lichen planus. They do not itch, however, and there are none to be seen on the mucosæ. They are thickly set on the forearms and thighs and less thickly on the trunk. The larger lesions, chiefly on the trunk, have become complete rings, raised bluish-red with a flat, fawn-coloured centre.

There is a collection of papules on his right shin where the skin is congested and thick and which followed a graze a week or so before the lesions appeared on the wrists. There are some fine delicate rings on the penis. There is no glandular enlargement detectable and he feels well. Wassermann negative.

Every effort will be made to follow the subsequent history of this case.

The lesions have been present for twelve weeks and it is early to say what they are going to do at this stage. Their annular lichen planus-like appearance has persuaded most members to regard the case as lichen planus, in spite of certain points slightly against that diagnosis.

Dr. Brian Russell: I think Dr. Whittle's case might be lichen planus.

The Chairman: I certainly thought it was an annular lichen planus.

POSTSCRIPT (30.8.46).—He states that the eruption has now almost disappeared, there being only a few spots left on the hips, and no fresh spots have appeared. The treatment given was liq. arsenicalis minims 5 to 8 t.d.s. for three months. The diagnosis of lichen planus is the more likely.—C. H. W.

R. G. Cochrane, M.D., F.R.C.P., read a paper on: The Significant Cellular Changes in the Corium in the Pathology and Diagnosis of Leprosy.

Section for the Study of Disease in Children

President—Professor NORMAN B. CAPON, M.D.

[April 26, 1946]

Multiple Achalasia, Vertebral Defects and Retarded Growth.—JOHN APLEY, M.D., M.R.C.P.
(by permission of Professor C. BRUCE PERRY).

F. C., at the age of 6, is a puny edition of his normal younger brother, who is only 3 years old (fig. 1).

There are four salient features in the history, and with each a physical abnormality is associated. Their significance can best be emphasized by considering each of these aspects in turn.

(i) *Development.*—There was some delay in passing the customary milestones of physical development. Now, at the age of 6, though the head is the anticipated size for age, the boy is 4 to 5 in. shorter than the average and is of slight build. His proportions are not, however, typically infantile; as an instance, the height is exceeded by the arm span. X-ray of the wrists indicates that skeletal development is barely within the lowest limit of normality.

Mentally bright, I.Q. normal. Psychiatric examination also shows no significant deviation.

(ii) *Enuresis.*—He has always been incontinent and precipitate of urine. Six months ago he came up to hospital with a bladder distended to the umbilicus, and suffering from overflow incontinence. After spinal anaesthesia up to the level of the fifth dorsal vertebra, the distension slowly receded, but the original incontinence and precipitancy were not appreciably relieved. He passes an average amount of normal urine. Intravenous pyelograph normal. Mr. Wilfrid Adams considered the dysfunction was in the nature of an achalasia.

(iii) *Encopresis.*—Though the patient has always been constipated, he has no control over defaecation. He suffers from attacks of abdominal pain and distension, and at these times the constipation is extremely marked. *Barium enema.*—Typical megacolon, with dilatation extending down to the anal sphincter. Unfortunately the spinal anaesthetic had no effect on the lower bowel symptoms.

(iv) *Vomiting.*—Occasional vomiting soon after eating, and not associated with discomfort or malaise. At the age of 3 he vomited after every meal for several weeks. Furthermore, he seems unable to eat more than a small amount at any meal. *Barium swallow.*—Stomach and duodenum normal but oesophagus enlarged.

Thus, four abnormal findings were directly suggested by the history. In addition, there is a dimple in the skin over the lower sacrum, and a tuft of hair over the upper

dorsal spine (fig. 2). These indications of the possibility of underlying vertebral defects were borne out by tomographic X-rays, which reveal neural arch anomalies at C6 and 7, at L3, 4 and 5, and at S1, 2 and 3 (fig. 3).



FIG. 1.—Contrast between patient, aged 6, and on his left his younger brother, aged 3.



FIG. 2.—To show dimple over lower sacrum and tuft of hair over upper dorsal spine.



FIG. 3.—Neural arch anomalies at L3, 4 and 5, and S1, 2 and 3.

Comment.—The importance of the case lies in the attempted demonstration that hypothalamic dysfunction may be concerned in the pathogenesis of achalasia.

It is well known that, in one individual, two pathologically enlarged viscera may be present simultaneously. Thus, megacolon and mega-oesophagus may occur together (Correia Neto, 1942), and a large bladder is found in an appreciable proportion of cases of megacolon (Adamson and Arid, 1932). The accepted view is that these and similar "mega"-conditions result from achalasia, which is itself produced by autonomic imbalance. Since this imbalance may conceivably originate in any part of the wide territory covered by the autonomic system, it may be possible to localize the primary focus.

In the present case there are two alternative sites to which the additional evidence points. The first is in the spinal cord. Both the bladder and large intestine are innervated from autonomic centres in the upper lumbar and mid-sacral regions. At the approximate levels of these spinal centres there are vertebral defects which may indicate underlying anomalies of the cord. But the correspondence is no more than approximate, and, moreover, the general retardation of growth could hardly be attributed to cord defects. For these reasons, in the search for a single location for the primary disturbance, the lesion must be placed at a higher level in the central nervous system. If this view is correct the vertebral defects are no more than an indication of coincidental developmental errors elsewhere.

As for the second possible site, there is convincing evidence that centres in the cerebral cortex and hypothalamus are concerned in the regulation of autonomic activity. Worster-Drought and Shafar (1940) suggest that developmental defects of these centres might result in corresponding gastro-intestinal anomalies, and the same authors and others (Watts and Uhle, 1936) postulate a central origin for megacolon and related bladder conditions. In the present case any cortical defect can, presumably, be eliminated because of the normal intelligence of the patient. The possibility of a hypothalamic defect remains, however, and this would suffice to explain adequately not only the autonomic imbalance but also, in the light of recent evidence (Riddoch, 1938, and Dott, 1938), the general retardation of growth.

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Hypertensive Retinopathy in a girl aged 10 years 11 months.—JAMES ROBERTSON, M.B., B.S. (by courtesy of Dr. R. LIGHTWOOD).

R. J., female. Admitted 2.4.46.

History.—Attacks of nausea and vomiting associated with headaches for the past year, at first occurring every three months but becoming more frequent; occurring weekly at time of admission and lasting about twenty-four hours. Headaches frontal, worse on right side and accompanied by giddiness. Nausea and loss of appetite during attacks, and occasional vomiting. She tires easily and sleeps badly with twitching of limbs. Getting thinner during last two months. Always thirsty and has polyuria, having to pass water two or three times during the night. No pain or burning on micturition.

Past history.—Measles, whooping-cough and chicken-pox. When aged 2 years had rickets with bow legs; these were fractured and reset. Frequent coughs and colds but no history of scarlet fever. Two years ago she injured her vulva by falling on a spike.

Family history.—Parents and two sisters well. An aunt has "blood-pressure".

On examination.—Pale girl with sallow complexion. Average height and intelligence but rather quiet.

Central nervous system.—Fundi show marked hypertensive retinopathy, with swollen oedematous discs. Retinal arteries are narrowed, veins engorged. Some "nipping" of veins. Star-shaped figures at both maculae more marked on right, and many other patches of exudate which are not of typical "cotton-wool" variety. A few scattered small hæmorrhages.

Cardiovascular system.—P. firm and regular. Cardiac impulse $\frac{1}{4}$ in. outside mid-clavicular line. Second apical heart sound slightly accentuated, otherwise sounds are normal. B.P. 240/170.

Urinary system.—Left kidney just palpable, seems small, is not tender. Right kidney not palpable. Urine S.G. 1015, reaction acid; albumin ++; no sugar; deposit shows epithelial cells, pus, hyaline and cellular casts.

Investigations.—3.4.46: Blood urea 39 mg./100 c.c. 11.4.46: Urea concentration test (1) 1.8 grammes, (2) 2.0 grammes, (3) 2.0 grammes, (4) 2.3 grammes % urea. 13.4.46: Bacteriological report of catheter specimen urine: Film—pus cells ++ and a few R.B.C. Cultures—coliforms ++++. 12.4.46: Blood-count: Hb. 100% (14.8 grammes/100 c.c.) Haldane. R.B.C. 4.8 million. C.I. 1.0. Size 7.1 μ . W.B.C. 15,000 (polys. 59%, lymphos. 32%, monos. 9%). 8.4.46: Urography—Right kidney normal, left kidney hydronephrotic probably. 20.4.46: Retrograde pyelography, L. kidney, large pelvis, single calicle pattern. No features suggestive of hydronephrosis.

The child has been given a full course of sulphonamides and at present the urine is sterile.

Since demonstrating the case differential ureteric catheterization showed the following urea concentration tests:

Left kidney: One hour after urea 1.5%; three hours after urea 2.2%. Deposit: R.B.C. and occasional leucocyte. Culture: Few *Staph. albus* and faecal streptococci.

Right kidney: One hour 0.5%. Deposit: R.B.C. only. Culture: Sterile.

Insufficient urine was obtained from the right kidney after one hour for further estimation as the catheter became blocked.

Following this procedure the girl had a prolonged attack of hypertensive encephalopathy lasting five days. Blood-pressure 260+/220, severe headache, vomiting and oliguria.

In view of the history of frequency, presence of pus and *B. coli* in the urine, and hypertension with hypertensive retinopathy, a diagnosis of chronic pyelonephritis with hypertension in a malignant phase was made. Chronic nephritis was considered unlikely because of the good renal function. The vulval injury is a possible ætiological factor.

Treatment.—Investigations have shown that both kidneys were affected. Removal of one or other kidney would therefore be ineffectual. In an attempt to lower the blood-pressure and intercept the vicious circle of malignant hypertension by producing Addison's disease, bilateral adrenalectomy is being performed. It is proposed to remove the whole of the right adrenal and the major portion of the left, leaving a small amount of adrenal tissue for further regeneration.

On 20.5.46 the right adrenal was removed and a right lumbar sympathectomy performed removing the coeliac ganglion, and the greater, lesser and least splanchnic nerves. The right kidney was found to be small, firm, irregularly pitted and scarred. It was decapsulated and a biopsy taken. The patient survived the operation well with no untoward reactions and no lowering of blood-pressure.

Postscript.—On 13.6.46 the second operation was performed. Three-quarters of the left adrenal was removed and left lumbar sympathectomy performed exactly as on the right side; the left kidney appeared normal. It was decapsulated and biopsy taken.

As a prophylactic measure 5 c.c. eucortone were given b.d. starting on the day of

dorsal spine (fig. 2). These indications of the possibility of underlying vertebral defects were borne out by tomographic X-rays, which reveal neural arch anomalies at C6 and 7, at L3, 4 and 5, and at S1, 2 and 3 (fig. 3).



FIG. 1.—Contrast between patient, aged 6, and on his left his younger brother, aged 3.



FIG. 2.—To show dimple over lower sacrum and tuft of hair over upper dorsal spine.



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The hands: In both hands there is complete fusion of the soft tissues of all digits forming a solid conical mass. This mass is fixed to the proximal part of the hand in a position of semiflexion, there is no movement present in the metacarpophalangeal joint region or in the mass itself. A shallow groove serves to demarcate the thumb, which is fused in the position of opposition, and a second groove demarcates the distal portion of the ulnar digit. The nails are fused into a continuous band across the mass, this band being deeply grooved in the positions already noted. Wrist-joints and other parts of the upper extremities are normal.

The feet: All digits on both feet are fused. There is no definite groove demarcating the great toe, but there is club-shaped thickening representing the great toes. There is a continuous nail band as in the hands. There are no movable joints between phalanges and metatarsals (figs. 1, 2, 3).



FIG. 1.



FIG. 2.



FIG. 3

Acrocephaly-Syndactyly.

X-ray appearances.—Skull: The base of the skull is very short antero-posteriorly. The pituitary fossa is shallow, there is marked increase in size of the greater wings of the sphenoid. The orbital plates of the frontal are short. The petrous bone is small and on a lower level than normal. A fissure is visible between the basi-occipital and basisphenoid bones. The height of the vault is greater than normal, $\frac{3}{4}$ in. greater than control. There is extreme thinning of the bone with linear striations in the frontal and parietal regions and disappearance of the inner table. In the occipital region the thickness of the skull is almost normal but there are "digital impressions". The coronal suture is not visible, and the lambdoid suture is poorly defined.

Hands: In both hands five normal metacarpals are present. The phalanges are represented by irregular masses of bone which are fused to each other. Five of these bony masses can be identified in the right hand and six in the left.

Feet: In each foot the three outer metatarsals appear normal but the inner two are fused, the first metatarsal being very short and branching off the second about one-third of its length from the proximal end. In the right foot there are three small distal bones on the outer side, and three irregular shaped proximal bony masses representing the phalanges, to the third of these is attached another irregular bone which represents the proximal phalanx of the second toe, but there is no corresponding distal phalanx. The phalanges of the great toe are represented by a fused mass of bone. In the left foot there are three small bones representing the three outer distal phalanges. The proximal phalanges are represented by three bony masses, each of which suggests fusion of several small bones and corresponds less to the metatarsal arrangement than in the right foot.

REFERENCE

GREIG, D. M. (1926) *Edinb. med. J.*, N.S., 33, 189.

the second operation. On the fourth day after operation, the girl had a puffy face and there was a good deal of water retention. The eucortone was discontinued and the œdema vanished.

After operation, the blood-pressure fell immediately to 100/60, rising slowly during the next four days to 184/160. At this point the eucortone was discontinued. During the next fortnight the blood-pressure gradually fell to 134/100. On July 1 there was a small rise to 160/120 and an immediate fall to 140/110 where it remained.

The child was seen again on 16.9.46. Blood-pressure 160/120. Urine sterile. No albumin or deposit. She was very well and gaining weight, and completely symptom-free since the operation. Fundi: Discs clear, no papilloedema. The exudates remain but are smaller, whiter and sharply defined. No hæmorrhages or nipping of veins.

Biopsy results.—Right kidney shows some periglomerular fibrosis. The glomeruli are a little reduced in size though a rather large one is present. On the whole there are only a few ischæmic changes.

Left kidney shows marked thickening of small arteries. Scanty sclerosed glomeruli with areas of interstitial fibrosis and tubular atrophy.

Right suprarenal normal. Left suprarenal shows large amount of cortical lipid. Arteries thickened.

Exophthalmic Goitre in a Child Aged 11 Years.—W. R. MAY, M.R.C.S., L.R.C.P. (by courtesy of Dr. REGINALD LIGHTWOOD).

J. M., aged 11 years 6 months. No family history of thyroid disease.

Personal.—Resident in London except during war years (one year in Wales, eight months in Hayes (Middlesex), and two years in Reading).

Present illness.—Admitted St. Mary's Hospital April 9. For two years mother has noticed she has been restless and excitable. For six months she has complained of headaches and mother noticed "staring". Fullness of the throat for one month and increased sweating and appetite.

On examination.—Height 4 ft. 9 in. Weight 5 st. 6 lb. Restless and thin. Obvious exophthalmos right more than left. Diffuse enlargement of thyroid gland. Neck measurement $11\frac{1}{4}$ in. Sexual development—breasts undeveloped; no pubic hair. Slight slow tremor of fingers and tongue. Blood-pressure 150/70. Urine—sugar trace. Blood-count: Hb. 105% (Haldane). Size 7.0 μ . W.B.C. 7,500 (polys. 62%, lymphos. 30%, monos. 8%).

Treatment commenced with methyl thiouracil 0.1 gramme daily increasing to 0.1 gramme three times daily. No toxic manifestations observed to date.

Acrocephaly-Syndactyly.—BERYL D. CORNER, M.D.

This case shows a severe degree of almost symmetrical syndactyly of hands and feet associated with gross abnormality of the skull, it has therefore been entitled acrocephaly-syndactyly as it is a typical example of Apert's syndrome. The condition of the skull would appear to fall into the group of cases described by Greig (1926) as true oxycephaly.

M. C., female, aged 6 months. First child, born after normal pregnancy by Caesarian section owing to failure of engagement of the head in the pelvis. Mother aged 41 years, father 43 years. Birth-weight $7\frac{1}{2}$ lb. Abnormality of head and extremities noticed at birth.

No family history of congenital abnormalities.

Examination.—The child is healthy and of normal size for her age. Sight and hearing appear normal, and mental development seems average.

The head: Appearance of the head is markedly brachycephalic with flat occipital region and shortened antero-posterior diameter. The height of the skull is much increased, maximum being just behind the anterior fontanelle. The orbits are shallow and separated by an abnormally broad depressed bridge of the nose, they slope downwards and outwards. Supra-orbital ridges are poorly defined, and above them is a deep groove passing across the whole forehead. The upper part of the frontal bone shows marked forward bulging which overhangs the face. The metopic suture is open to the glabella, and the anterior fontanelle is situated far forward. The posterior fontanelle is closed and no other sutures can be palpated. The superior maxillæ are small and depressed, the nose is short and there has been partial nasal obstruction with snuffles since birth. There is bilateral exophthalmos with divergent strabismus, but no evidence of optic atrophy or abnormality of the retina. Owing to the short mouth, the tongue protrudes continuously. The lower jaw protrudes slightly and appears large in comparison with the rest of the face.

Head measurements: Circumference $16\frac{1}{2}$ in. External auditory meatus to highest point of skull 7 in. Glabella to highest point $4\frac{1}{4}$ in.

The hands: In both hands there is complete fusion of the soft tissues of all digits forming a solid conical mass. This mass is fixed to the proximal part of the hand in a position of semiflexion, there is no movement present in the metacarpophalangeal joint region or in the mass itself. A shallow groove serves to demarcate the thumb, which is fused in the position of opposition, and a second groove demarcates the distal portion of the ulnar digit. The nails are fused into a continuous band across the mass, this band being deeply grooved in the positions already noted. Wrist-joints and other parts of the upper extremities are normal.

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Primary Hyperplasia of the Parathyroids in a Boy Aged 8 Years.—R. J. PUGH, M.B., M.R.C.P. (for W. G. WYLLIE, M.D., F.R.C.P.).

The patient was under observation in hospital for a period of five months prior to diagnosis, and gave a history for three months preceding admission, before which he had been in good health. An insidious onset of anorexia, increasing polydipsia with enuresis, occasional vomits and frequent pains in the head, abdomen and behind the knees, was reported. There was progressive muscular weakness so that the patient was no longer able to walk, and had to pull himself to his feet. Previously there had been an attack of tonsillitis at the onset, but the only other illness was measles. The parents and two siblings were healthy.

Apart from extreme lethargy and evidence of recent weight loss, no significant findings were made on examination, but subsequently he frequently exhibited nuchal stiffness and frontal headache.

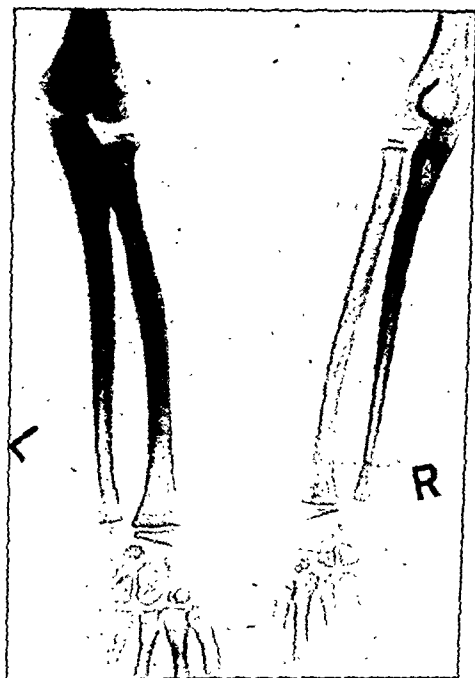


FIG. 1.—Radiograph of patient's arm (R) with control of the same age (L). (Exposure on the same plate.)



FIG. 2.—Micrograph showing pseudo-alveoli and giant nuclei. $\times 147$.

Initial findings.—Blood-count: R.B.C. 5,280,000; Hb. 85%; C.I. 0.81. W.B.C. 8,900 (50% polymorphs). B.S.R.: 47 mm. in one hour. C.S.F.: No abnormal findings; pressure 70 mm. Urine: Acid; alb. 15 mg.%; no deposit; sterile; sugar absent. Blood urea: 33 mg.%.
X-rays: Nothing abnormal.

1:1000 Mantoux: Very strongly positive. B.P. 95/65.

Course in hospital.—During the next five months the symptoms continued unabated; the fluid intake averaged 55 oz. daily, while the intermittent bouts of vague pains increased in severity sometimes with tenderness of the limbs and back on turning in bed for washing. Anorexia and ready fatigue were extreme. No evidence of active tuberculosis could be found radiologically or in gastric washings. There was no benefit from posterior pituitary extract injection. The blood urea remained normal. Intravenous pyelography was attempted on three occasions, but renal concentration was lacking. Routine agglutination reactions were uniformly negative. The erythrocyte sedimentation tube remained around 60 mm. in one hour.

The possibility of a tuberculoma in the floor of the fourth ventricle was considered, and a normal ventriculogram was performed by Mr. Wylie McKissock.

Attention was drawn to the skeletal system by the appearance of rarefaction in the necks of the femurs, and by the necrotic nature of the cranial burrholes. Histology of

the skull showed extreme osteoporosis. Urine gave a heavy precipitate with Sulkowitch reagent.

Blood chemistry.—Serum calcium 18.8 mg.%; inorganic blood phosphorus 2.8 mg.%; alkaline serum phosphatase 93 units.

Operation.—An exploration of the parathyroids was undertaken by Mr. Charles Donald, and revealed a tumour the size of a large hazelnut, purple in colour, inferior to the thyroid capsule beneath the sternal notch. This was removed. (Histological report in detail, see addendum.)

Progress.—There was immediate amelioration of many symptoms, including anorexia, pain in movements of limbs, headache, and neck stiffness. The fluid intake dropped to 25 oz. daily, and there has been no further enuresis. The alkaline serum phosphatase continued greatly raised (107 and 87 units respectively). The blood calcium fell more slowly over the course of forty-eight hours, to 8.9 mg.%, and in six days was down to 6.5 mg.%. There was no tetany, and the level was restored by high calcium intake with the addition of 10,000 units of vitamin D daily. There has been a gain in weight of over 4 lb. in less than three weeks, with improvement in muscle tone. The B.S.R. remained raised and was 61 mm. in one hour three weeks after operation, when the blood chemistry revealed: Serum calcium 9.4 mg.%; inorganic blood phosphorus 3.3 mg.%; alkaline serum phosphatase 62 units.

Progress satisfactory. We are indebted to Dr. W. W. Payne for the biochemical investigations, and to Dr. Martin Bodian for the histological examination.

ADDENDUM

Histological report.—Predominant cell type of transitional principal variety with few isolated oxyphil cells. Between them many giant nuclei are present as well as few cells with multiple nuclei and mitotic figures. Oedema, congestion and frank hæmorrhages lead to breaking up of cell columns and to formation of "pseudo-alveoli". Much droplet glycogen is present in the cells. There is no evidence of neoplastic growth. The findings indicate hyperplasia of the parathyroids.

Tumour of the Optic Chiasm and Nerve Sheaths in a Girl Aged 2 years 9 months, Showing Some Manifestations of Neurofibromatosis.—R. J. PUGH, M.B., M.R.C.P. (for BERNARD SCHLESINGER, M.D., F.R.C.P.).

Patient has exhibited progressive proptosis of the left eye for the last five months, with increasing impairment of vision, difficulties in feeding, and weight loss. For the last month there have been frequent transient left frontal head pains with hyperparæsthesia over the left trochlear region. There was no history of vomiting, or other neurological symptoms.

Her father shows patches of café-au-lait pigmentation about the trunk, and a single molluscum in the neck.

Examination revealed a wasted child weighing only 22 lb., with many café-au-lait patches on the trunk, and a soft nodule on the scalp. The left eye is markedly proptosed, the right slightly so. Optic fundi show advanced atrophy on the right while the left is of normal colour and vascularization, but is displaced forwards about 6 dioptries.



FIG. 1.—Radiograph showing flattening of pituitary fossa with erosion of anterior clinoid processes.



FIG. 2.—Enlarged right optic foramen (indicated by arrow).

Stereoscopic skull X-rays reveal thickening of the greater wing of the sphenoid with erosion of the anterior clinoid processes, and gross widening of both optic foramina to about three times normal size for age.

Cerebrospinal fluid examination gave a pressure of 95 mm., a protein content of 90 mg.%, cells absent, sugar 65 mg.% and chlorides 740 mg.%. Wassermann reaction of the blood and C.S.F. was negative. Mantoux: 1:1000 negative.

Biopsy of lump in subcutaneous tissues of scalp was reported as having the histological appearance of a soft fibroblast undergoing mucoïd degeneration (Dr. Martin Bodian).

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Familial Hæmolytic Anæmia.—CHARLES PINCKNEY, F.R.C.P.

D. R., male, aged 6 months. Sent to hospital with history of bronchitis and pallor since birth, which has increased recently. A first baby, birth-weight 7 lb. 10 oz., normal labour, not breast-fed. Taking well till previous week when developed bronchitis.

Father had splenectomy; report on grandfather as having had splenectomy.

On examination.—Marked pallor, signs of generalized bronchitis, spleen enlarged and firm, half-way to umbilicus.

12.3.46: Admitted to hospital. Investigations: Hb. 35%, reticulocytes 30%. Fragility test—commencing hæmolysis in 0.72% saline. Blood transfusion given: Hb. raised to 100%.

Discharged well but spleen still enlarged.

Seen again in Out-patients, 23.4.46; weight gain satisfactory, but increase of anæmia present. Investigation showed R.B.C. 2,350,000; Hb. 40%; reticulocytes 1%. Admitted for further transfusion and splenectomy.

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Pneumococcal Empyema.—Treated with Penicillin.—M. E. HUGHES, M.B., B.S. (for H. M. M. MACKAY, F.R.C.P.).

B. D., male child aged 8 months. Admitted 22.3.46 with a history of a febrile illness and cough seven weeks previously, a recurrence of symptoms and "heavy" breathing two weeks before admission.

On admission T. 99.4°F.; P. 144; R. 46. Child was very ill and pale with signs of a large effusion in the left side of his chest with displacement of the heart to the right. Radiography confirmed the presence of a large effusion on the left side and the heart was displaced completely across the mid-line into the right side of the chest. Aspiration produced 80 c.c. of thick green pus which on culture grew a penicillin-sensitive pneumococcus.

The child was treated with daily aspirations and intrapleural penicillin, using 40,000 units in a volume of saline equal to half the volume of pus aspirated on each occasion. The volume of pus decreased daily and on the fifth day no pus was obtained, and on two subsequent occasions no pus was obtained.

Radiologically the left side of the chest cleared steadily. Convalescence was interrupted by the development of a pneumonic consolidation at the right base which was treated with systemic penicillin and cleared rapidly. The anæmia failed to respond to iron therapy and a transfusion of 250 c.c. of blood was given.

The child's condition improved rapidly and he gained in weight. On discharge there were no abnormal physical signs in his chest and X-ray showed only very slight loss of translucency at the left base.

Arachnodactyly with Amyoplasia Congenita.—E. M. KINGSLEY-PILLERS, M.B., B.Chir. (for H. M. M. MACKAY, F.R.C.P.).

David L., born 27.2.46. The baby was first seen at 10 days old and had not seemed normal since birth. The arms were flexed at the elbow-joints and could not be extended beyond 90 degrees. The knees were flexed with marked limitation of extension. The hands were large with long spidery fingers and the feet were long and thin. The foot

could be easily dorsiflexed on to the shaft of the tibia. There was marked kyphosis in the lower thoracic and lumbar regions. There was no evidence of abnormalities in the eyes or in the heart. The pregnancy and labour were normal and the birth-weight was 6 lb. 10 oz. The amniotic fluid was normal in amount. There is no parental history as the baby is illegitimate. The W.R. and Kahn were negative. The X-ray of the long bones were normal and the electrical reactions of the muscles were normal in the biceps, triceps and hamstrings, but there was no response to faradism or galvanism in either quadriceps. Treatment by daily passive movements to the limbs has been successful and movements are considerably improved.

The large hands with long tapering fingers and the large strip-like feet present features typical of arachnodactyly but the fixation of the elbows and knees in flexion at birth and the thinness and lack of development of the muscle groups of the limbs are usually noted in cases of amyoplasia congenita. Cases of arachnodactyly are commonly associated with other congenital deformities but in this case we have been unable to find any abnormality in the heart or the eyes.

Osteomyelitis and Nephritis.—R. M. TODD, M.D., M.R.C.P., D.C.H.

Albert G., aged 7½ years.

19.2.46: Blisters on right heel. 22.2.46: Pain in right leg and difficulty in walking. 23.2.46: Feverish, restless and delirious.

24.2.46: Admitted to hospital, T. 103°F. Semicomatose. Swelling and tenderness of right leg below knee, slight erythema of overlying skin. No lymphangitis or lymphadenitis. Blisters of foot healed. Systemic penicillin commenced (240,000 units *per diem*). Lumbar puncture—n.a.d. Blood culture sterile. Urine n.a.d. Hb. 82%; W.B.C. 11,200; polys. 80%. W.R. and Kahn negative.

25.2.46: Delirious. Refusing fluids. Intravenous glucose saline commenced. 26.2.46: Sulphamezathine started. 27.2.46: X-ray leg—no bony lesion.

1.3.46: Right leg splinted. Drip discontinued. General condition improved. Co-operative. 4.3.46: Sulphamezathine discontinued (total 50 grammes).

5.3.46: Urine—S.G. 1028; acid, albumin +. Many red cells and granular casts. No organisms. Blood urea 40 mg.%. Low protein diet.

14.3.46: Incision and drainage right leg. Large amount of pus obtained (sterile). Penicillin discontinued (total—4,320,000 units). X-ray: Necrosis and periostitis. 28.3.46: Leg put in plaster. Serum proteins normal. Blood urea 56 mg.%. 12.4.46: Still has macroscopic blood in urine. Granular casts present.

22.4.46: Urine (Ward test). No albumin. No blood.

24.4.46: Plaster removed—wound healed. X-ray: Marked periosteal reaction, necrotic area in upper third of tibia. Replastered. Blood urea 33 mg.%. Plasma proteins normal. B.P. 110/65. Urine: No casts, few R.B.C.

Comment.—This case presented two interesting points:

(1) The nature of the disease—whether a cellulitis with secondary periostitis, or a primary osteomyelitis. Streptococci are the common cause of the former, and staphylococci of the latter condition. No organisms were isolated either from the blood, pus or urine probably due to early treatment with penicillin. The nature of the pus (thin) may also have been influenced by penicillin.

(2) What was the nature of the nephritis? Was it a focal nephritis, a diffuse suppurative nephritis or an acute glomerulo-tubular nephritis? The absence of organisms and white cells from the urine, and the onset of the nephritis two weeks after a septic process are in favour of the last possibility.

Suppurative Arthritis Treated by Aspiration and Penicillin Replacement (Three Cases).—

A. D. BARLOW, M.R.C.P.

Meningococcal Meningitis with Suppurative Arthritis.—(Under D. PATERSON, F.R.C.P.)

P. L., male, aged 2½ years. Admitted to hospital with meningitis after a two-day history of fever, irritability and purpuric rash. Seriously ill though not comatose.

Lumbar puncture yielded a purulent fluid from which meningococci were cultured.

Given penicillin 10,000 units intrathecally on alternate days, and sulphamezathine 1 gramme four-hourly.

Temperature fell from 103°F. to normal in twenty-four hours, and remained normal until the fifth day when it rose to 102°F. He was found to have painful swelling of the left knee from which a purulent fluid was aspirated. On the following day the left elbow was swollen, and the day after, the right knee and elbow. On no occasion could any organism be cultured from the joints. The L. knee and L. elbow subsided after single aspiration and penicillin replacement; the right elbow recovered spontaneously; the right knee required aspiration every few days for two weeks. Besides local penicillin he has had 5,000 units intramuscularly four-hourly for eighteen days.

He now has full movement in all joints, and a little fluid still in the right knee.

Stereoscopic skull X-rays reveal thickening of the greater wing of the sphenoid with erosion of the anterior clinoid processes, and gross widening of both optic foramina to about three times normal size for age.

Cerebrospinal fluid examination gave a pressure of 95 mm., a protein content of 90 mg.%, cells absent, sugar 65 mg.% and chlorides 740 mg.%. Wassermann reaction of the blood and C.S.F. was negative. Mantoux: 1:1000 negative.

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changes demonstrate that prenatal and neonatal glycogen metabolism differs from that occurring later. He considers that increased insulin sensitivity and probably faulty glycogenolysis to be operative, and not absolute hyperinsulinism.

In the newborn of the diabetic mother, hypoglycæmia may be responsible for severe reactions, convulsions, and collapse, but this is generally remedied by glucose feeds. Neonatal hypoglycæmia may be intensified in its effects by intracranial injury or adrenal hæmorrhage.

Rector and Jennings observed the occurrence of hypoglycæmia with convulsive effects in children, aged 1 to 3 years (11 cases). They suggest it is due to intermittent functional hepatic disorder with temporary depletion of glycogen reserve and that most cases are amenable to conservative management, especially a diet high in carbohydrate and that the prognosis is infinitely better than it is for older patients with hypoglycæmia of organic origin. Whilst recognizing that hypoglycæmia is not a frequent cause of convulsions in childhood they suggest that blood sugar studies should be made in cases of obscure convulsion disorder in childhood.

Graham and Hartmann report a case of a girl aged 1 year, with blood sugar 18 mg.%, who was benefited by partial pancreatectomy.

In hypoglycæmia the symptoms and signs may be considered as an ordered depression of the cerebral levels from the higher to the lower, and the clinical effects would seem to bear a relationship to a rate of fall as well as a degree of fall in the blood sugar. The symptoms may vary in the same patient under the same degree of hypoglycæmia. There is considerable variation in individual sensitivity to insulin. Sometimes even though the blood sugar may decline to 30 mg.% reaction may be delayed up to thirty to sixty minutes and in fact may synchronize with a reactionary rising level of blood sugar. Notably also, flushing and sweating varies considerably in the patients. There is no doubt that there is a personal cerebral sensitivity in the hypoglycæmia state, and this may be compared with alcohol intoxication and the behaviour patterns may be considered in relation to hypothalamic responses.

CASE I.—M. T. Spontaneous hypoglycæmia. First baby, 40 weeks' pregnancy, birth-weight 7 lb., normal delivery. Eight hours' labour. Admitted on 30.1.46, aged 4 weeks, with a history of being quite well until two days previously when he had gone off his feeds and become constipated. He had had several small convulsions on the day of admission. He was found to have some umbilical sepsis with a palpable liver and inflammation of the throat and ears. A tentative diagnosis of neonatal infection was made and treated with sulphonamide and penicillin. Intravenous infusions of 5% dextrose were given from 30.1.46 to 1.2.46. Frequent convulsions occurred between 3 to 6.2.46, during which the calorie value of his feeds was increased although the sugar remained at the same level (50 grammes per day). Infantile tetany was suspected, but the blood calcium was normal (10.7 mg.). On discharge on 12.2.46 he had gained weight from 6 lb. 5 oz. to 6 lb. 12 oz. and was chiefly breast-fed with a complementary feed containing 7% carbohydrate. In hospital he was fed at three-hourly intervals with the 3 a.m. feed omitted, but on his return home the 12 midnight feed was also omitted.

Readmitted on 15.2.46 with a history of having had several convulsions per day since discharge three days previously, although he had been taking his feeds well. On examination he was apparently unconscious with twitching of his limbs and face. Respiration was very irregular and shallow. No signs of infection were found. As he was not taking by mouth, intravenous infusions of 5% dextrose were given on February 15 and 16, 1946. The epileptiform state ceased during the night of the 15th-16th. Lumbar puncture on the 16th and 21st did not show any diagnostic signs of meningitis or of cerebral hæmorrhage; the protein was 30 mg. per 100 ml. and the sugar was absent.

The convulsions continued, about 6 to 7 being observed per day. He was noticed to sweat profusely during these attacks of twitching and this together with the low C.S.F. sugar suggested a diagnosis of hypoglycæmia. Blood sugar on 1.3.46 was 23 mg.%, the specimen being taken three hours after a feed. The feeds were increased from 42 grammes sugar daily to 70 grammes including a feed at 12 midnight; the convulsions were controlled. On 5th the response to an injection of adrenalin, 2 ml. of 1/1,000 solution was found from blood-sugar readings to be normal. The convulsions persisted in spite of increasing the feed on 13th to 50 grammes sugar daily. On 19th a diurnal glucose curve gave low readings falling to 20 mg.% at midnight, so the feeds were increased to 68 grammes sugar daily with a feed at midnight. As he had no fits for a month he was allowed home. Just before discharge the interval between feeds was increased to four hours and the midnight feed omitted. He returned to the Out-Patient Department a week later having had further convulsions. The sugar content of the feeds was increased to 87 grammes per day; three-hourly, with a feed at midnight. While in hospital he never showed any intolerance to the high percentage of sugar in the feeds, and on this high carbohydrate appeared to be generally better, but diurnal blood-sugar readings showed moderate low level and undoubtedly hypoglycæmia was intermittently present.

The clinical progress has been poor despite high carbohydrate intake. The baby now shows evidence of cerebral damage and a condition of decorticate rigidity has appeared. Insulin depression curve on 68 grammes carbohydrate diet showed a minimum reading of 44 mg. The lowest blood-sugar diurnal variation—25 mg. Liver, viscera, n.d.

His mother's blood-sugar and glucose tolerance curves were found to be normal.

CASE II.—J. P. Spontaneous hypoglycæmia. Birth-weight 8 lb., forty-eight hours' labour. Possibly some cerebral damage at birth. Forceps delivery. At 2 days old, went limp, did

Suppurative Arthritis following Bronchopneumonia.—(Under W. G. WYLLIE, F.R.C.P.)

T. G., male, aged 4½ years. History of bronchopneumonia in March 1946 followed fourteen days later (27.3.46) by pain, stiffness and swelling in the left knee.

Admitted to hospital 1.4.46. On examination the chest was clear. The left knee contained fluid. Temperature 100°F.

Purulent fluid was aspirated from his knee, from which a hæmolytic streptococcus was grown. 10,000 units of penicillin were injected into his knee-joint, and he was given 10,000 units four-hourly intramuscularly for ten days.

After three days there was considerable improvement, and in eight days he was symptomless.

Suppurative Arthritis of Right Elbow following Mastoiditis.—(Under B. SCHLESINGER, F.R.C.P.)

J. D., female, aged 9 years.

Left mastoid operation two years ago.

27.2.46: Admitted to hospital with pain and purulent discharge from left ear, and swelling behind the ear.

Mastoid reopened and necrotic remains of mastoid air cells removed. Penicillin applied locally, 3,000 units four-hourly for five days. Wound healed satisfactorily. Discharged from hospital 20.3.46.

25.3.46: Right otitis media, which cleared in a few days on sulphonamide treatment.

On 2.4.46 she began to complain of pain in her right arm, and was readmitted to hospital on 7.4.46 with a temperature of 101°F. and signs of fluid in her right elbow. Aspirated fluid was purulent and grew a hæmolytic streptococcus. On the two days following admission penicillin (10,000 units) was injected into the joint, and she was also given 10,000 units four-hourly intramuscularly for ten days.

She became afebrile in four days, there was no further accumulation of fluid in her elbow, and she was discharged fit after seventeen days.

[May 25, 1946]

Spontaneous Hypoglycæmia in Infancy and Childhood

By A. V. NEALE, M.D.

IN the normal regulation of the blood sugar several factors are physiologically integrated, including hormones of the anterior pituitary gland, islets of Langerhans, adrenal cortex and medulla, glycogen-glucose interchange, tissue metabolism, renal threshold, diet, and possibly nervous mechanisms particularly in the hypothalamus.

The hormones of the anterior pituitary favour gluco-neogenesis, in opposition to insulin, and counteract the peripheral action of insulin in the tissues. In hypophysectomy there is a hypersensitivity to insulin with possibly hypoglycæmia.

The brain of the fœtus and of the newborn is probably less susceptible to permanent damage by anoxia. It is suggested that the tolerance of young dogs to anoxia and hypoglycæmia is related to relatively low cerebral metabolic rate, and an anaerobic source of energy. In the adult the reverse is the case, and is related to the greater susceptibility of the higher centres, and cerebral tissue to anoxia and hypoglycæmia. In fatal hypoglycæmia there is widespread degeneration and necrosis of nerve cells in the cerebral cortex, and basal ganglia, this being probably due to failure of vital oxidative processes from lack of substrate glucose and worsened by subsequent vasomotor disturbance.

Hypoglycæmia may occur in numerous clinical conditions including adrenal insufficiency; pituitary insufficiency, e.g. tumour, cyst, or atrophy; Von Gierke's hepatomegalia glycogenica; hypothyroidism; renal glycosuria and low carbohydrate diet; prematurity; and possibly in hypothalamic lesions. Parris and Ingram observed the occurrence of hypoglycæmia in animals with experimental lesions in the anterior hypothalamus, particularly in the neighbourhood of the paraventricular nucleus. There are cases of spontaneous hypoglycæmia in which the cause is not definite. True hyperinsulinism, e.g. islet tumour, is extremely rare in childhood.

Hypoglycæmia may occur in the newborn, during the first several days of life. This is probably due to imperfect endocrine regulation, with relative hyperinsulinism or defective glycogenolysis. Hartmann and Jaudon state that hypoglycæmia during the first four or five days of life occurs quite frequently in normal newborn infants, and seems to be due to an imperfectly developed regulatory mechanism which creates a state of functional hyperinsulinism.

Van Creveld observes that the glycogen of the newborn shows the interesting difference that relatively large amounts of adrenalin are required for its mobilization and various

changes demonstrate that prenatal and neonatal glycogen metabolism differs from that occurring later. He considers that increased insulin sensitivity and probably faulty glycogenolysis to be operative, and not absolute hyperinsulinism.

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CASE II.—J. P. Spontaneous hypoglycæmia. Birth-weight 8 lb., forty-eight hours' labour. Possibly some cerebral damage at birth. Forceps delivery. At 2 days old, went limp, did

not feed until 8 days old, sucked well at 14 days, progress thereafter good. At 8 months suddenly went limp. Remained so for three days. Recovered after further five days. At 1 year 3 months, sudden collapse. Remained limp for some days and improved on glucose. Several short attacks of this kind. A week or so later—vomiting, and screamed for two hours, and was noticed to be staggering about. Became very limp and then became deeply unconscious. Admitted to hospital in a stuporous state. Limbs flaccid, plantar reflexes extensor. C.S.F.—absence of sugar. Blood sugar 38 mg.%. Intravenous glucose given. Some minutes after glucose child became more awake, colour improved, movements more purposive. Child smiled, rubbed her nose, but did not speak.

Child feeds satisfactorily, and progressed well until a month later when hypoglycaemic attack occurred without convulsions. Thought to be asleep but could not be roused. Blood sugar 35 mg.%. Adrenalin 5 ml. of 1/1,000 sol. revived patient within ten minutes. This child has periodic spontaneous hypoglycaemic reactions often associated with vomiting, but no definite convulsions. Present condition satisfactory. Attacks only occasional. Diurnal variation showed minimal readings of 45 mg.%. Attacks very much less frequent. No clinical evidence of any visceral abnormality. Parents healthy. Other children in family healthy.

CASE III.—R. H. Spontaneous hypoglycaemia. Nutritional history normal. At the age of 3 years found in coma one morning. Clinical examination negative apart from toneless muscles, rapid feeble pulse. Became rapidly worse and appeared to be on the verge of death with breathing feeble and shallow. Blood sugar 26 mg.%. C.S.F. sugar 12 mg.%. Intravenous glucose given and 5 ml. of adrenalin which caused rapid improvement. Intravenous discontinued and child took food well for a time, and then refused entirely; blood sugar fluctuated at low levels. Insulin depression curve showed minimal reading of 47 mg. Was put on full diet and discharged home as satisfactory. Nine months later the boy was brought, in coma, to the Casualty Department. Two and a half ounces of glucose in water were passed into the stomach and in ten minutes consciousness was regained. No further attacks have occurred and the boy seems to have maintained improvement on a diet rich in fat and poor in carbohydrate. Present diurnal blood-sugar readings normal.

CASE IV.—P. M. I. Epilepsy with associated hypoglycaemia. Well until aged 10 years when menstruation commenced and slight convulsions synchronously. Occasional but definite epileptiform attacks occurred just before a meal and all occurred a few days after the end of a menstrual period. General physique and mental level good. Minimal blood sugar and diurnal variation 50 grammes %. E.E.G. showed definitely abnormal reading which is referred to as being of diffuse type rather than local, and therefore is in accordance with diagnosis of idiopathic epilepsy aggravated by hypoglycaemia phases.

CASE V.—J. M. Pituitary cachexia, with increased insulin sensitivity. No hypoglycaemia symptoms. At the age of 8 appeared in a grossly emaciated condition with weakness and all the signs of pituitary insufficiency. Pathologist's examination showed a cyst of the pituitary gland. Diurnal variation of the blood sugar showed minimal reading of 45 mg.

CASE VI.—M. B. Anorexia nervosa. No hypoglycaemia. In contrast with the case of J. M., in this patient—although similarly and grossly wasted—diurnal variation showed normal readings, and at no time any hypoglycaemia.

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The Treatment of Coeliac Disease with Vitamin B Complex and Liver Extract

By ERIC C. ALLIBONE, M.D.

ROSS (1936) showed that the administration of liver extracts improved the glucose tolerance in coeliac disease. ANDERSON (1945) had noticed that giving a mixture of five of the vitamin B fractions improved the appetite in this condition. MAY, McCREARY and BLACKFAN (1942) using both parenteral liver and vitamin B complex obtained rapid clinical improvement with a rise in the vitamin A absorption tests, the patients being kept on a normal diet. PATERSON, PIERCE and PECK (1944) using the same method as MAY *et al.* confirmed the clinical improvement in coeliac disease but did not obtain such good results in the vitamin A and oral glucose tolerance tests.

This paper records the results of the cases of coeliac disease treated in this hospital on the above lines. Thanks to the kindness of Professor Struthers of Montreal and Messrs. John Wyeth and Brothers Ltd., London, it was possible to get the same preparations as were used in America by MAY and his co-workers.

Method.—After the initial investigations, daily intramuscular injections of vitamin B (4 c.c.) alternating with liver extract (2 c.c.) were given. The duration of the course

was three weeks in the first 15 cases and was then raised to six weeks in a further 8 cases. After reassessment the patients were put on oral treatment consisting of proteolized liver, vitamin B complex, vitamins A, D, and C, and iron. Whenever feasible an ordinary ward diet was given. The duration of the oral therapy varied between six months and a year.

The diagnosis was made on the history, physical signs and stool analysis. The duodenal enzymes were not estimated as a routine. In no case, except one which proved fatal, were respiratory symptoms prominent or persistent, though 11 cases had signs on admission of a recent upper respiratory infection.

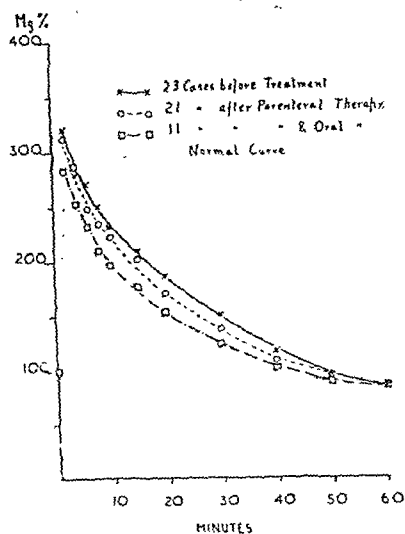


FIG. 1.—Composite intravenous glucose tolerance curves in coeliac disease.

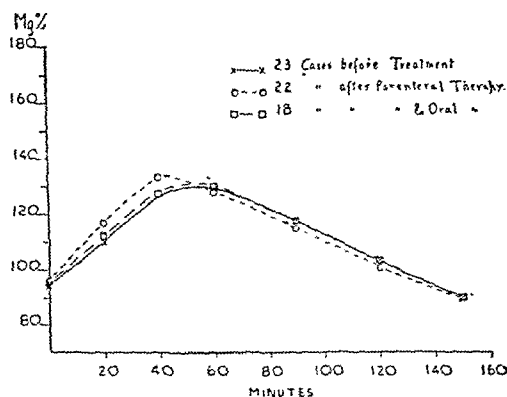


FIG. 2.—Composite oral glucose tolerance curves in coeliac disease.

The age of onset of symptoms varied from birth to 33 months with an average of 14 months. The average age at commencement of treatment was 3 years 5 months though, if 4 mild cases in older children were to be excluded, this figure was reduced to 2 years 2 months.

RESULTS

Twenty-three cases were investigated. Of these two died. One had recurrent attacks of bronchitis and contracted a fatal pneumonia while in another hospital. An autopsy was refused. It is possible that this case may have had a pancreatic fibrosis. The other, while on oral therapy, relapsed with diarrhoea followed by generalized weakness. A fortnight after the onset of the recrudescence he was admitted to hospital and died five days later. The post-mortem examination showed an enteritis, otitis media with a terminal bronchopneumonia. Histologically there was atrophy of the secretory tissue of the pancreas with increase of the connective tissue. There was no evidence of chronic bronchial suppuration. Tiny patches of demyelination of the posterior columns of the spinal cord with hydropic degeneration of the heart muscle suggested a diagnosis of beriberi. Dr. H. S. Baar, who performed the autopsy, was unable to say whether the pancreatic changes were primary or secondary.

Three cases defaulted after going home on oral therapy. Of the remaining 18 cases, 6 had to be put on a fat-free diet at the end of the course of parenteral treatment because their clinical condition was deteriorating. A further 4 were changed to a low fat diet as a result of the final assessment after six to twelve months' oral treatment, leaving 8 patients well enough to remain on an ordinary diet.

Although initially under height, growth occurred at the normal rate during treatment. A deficiency in weight was decreased. The figures for weight cannot be considered to be a reliable index of progress, owing to fluctuations in the bulk of the intestinal contents (Table I).

TABLE I.—AVERAGE HEIGHT AND WEIGHT IN COELIAC DISEASE.

	Before treatment	After treatment
Height, expressed as a percentage of the expected height for the age (12 cases) ...	88	90
Weight, expressed as a percentage of the expected weight for the age ...	71	76
Weight, expressed as a percentage of the expected weight for the height ...	91	96

not feed until 8 days old, sucked well at 14 days, progress thereafter good. At 8 months suddenly went limp. Remained so for three days. Recovered after further five days. At 1 year 3 months, sudden collapse. Remained limp for some days and improved on glucose. Several short attacks of this kind. A week or so later—vomiting, and screamed for two hours, and was noticed to be staggering about. Became very limp and then became deeply unconscious. Admitted to hospital in a stuporous state. Limbs flaccid, plantar reflexes extensor. C.S.F.—absence of sugar. Blood sugar 38 mg.%. Intravenous glucose given. Some minutes after glucose child became more awake, colour improved, movements more purposive. Child smiled, rubbed her nose, but did not speak.

Child feeds satisfactorily, and progressed well until a month later when hypoglycaemic attack occurred without convulsions. Thought to be asleep but could not be roused. Blood sugar 35 mg.%. Adrenalin 5 ml. of 1/1,000 sol. revived patient within ten minutes. This child has periodic spontaneous hypoglycaemic reactions often associated with vomiting, but no definite convulsions. Present condition satisfactory. Attacks only occasional. Diurnal variation showed minimal readings of 45 mg.%. Attacks very much less frequent. No clinical evidence of any visceral abnormality. Parents healthy. Other children in family healthy.

CASE III.—R. H. Spontaneous hypoglycaemia. Nutritional history normal. At the age of 3 years found in coma one morning. Clinical examination negative apart from toneless muscles, rapid feeble pulse. Became rapidly worse and appeared to be on the verge of death with breathing feeble and shallow. Blood sugar 26 mg.%. C.S.F. sugar 12 mg.%. Intravenous glucose given and 5 ml. of adrenalin which caused rapid improvement. Intravenous discontinued and child took food well for a time, and then refused entirely; blood sugar fluctuated at low levels. Insulin depression curve showed minimal reading of 47 mg. Was put on full diet and discharged home as satisfactory. Nine months later the boy was brought, in coma, to the Casualty Department. Two and a half ounces of glucose in water were passed into the stomach and in ten minutes consciousness was regained. No further attacks have occurred and the boy seems to have maintained improvement on a diet rich in fat and poor in carbohydrate. Present diurnal blood-sugar readings normal.

CASE IV.—P. M. I. Epilepsy with associated hypoglycaemia. Well until aged 10 years when menstruation commenced and slight convulsions synchronously. Occasional but definite epileptiform attacks occurred just before a meal and all occurred a few days after the end of a menstrual period. General physique and mental level good. Minimal blood sugar and diurnal variation 50 grammes %. E.E.G. showed definitely abnormal reading which is referred to as being of diffuse type rather than local, and therefore is in accordance with diagnosis of idiopathic epilepsy aggravated by hypoglycaemia phases.

CASE V.—J. M. Pituitary cachexia, with increased insulin sensitivity. No hypoglycaemia symptoms. At the age of 8 appeared in a grossly emaciated condition with weakness and all the signs of pituitary insufficiency. Pathologist's examination showed a cyst of the pituitary gland. Diurnal variation of the blood sugar showed minimal reading of 45 mg.

CASE VI.—M. B. Anorexia nervosa. No hypoglycaemia. In contrast with the case of J. M., in this patient—although similarly and grossly wasted—diurnal variation showed normal readings, and at no time any hypoglycaemia.

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Clinical Section

President—A. DICKSON WRIGHT, M.S., F.R.C.S.

[April 12, 1946]

Sarcoidosis.—K. N. V. PALMER, M.B. (for Dr. G. E. BEAUMONT).

F. N., housewife, aged 40. Married, 3 children, aged 14, 10 and 6, all well.

Family history.—Mother died aged 55 of carcinoma of the womb. Nothing else relevant. No contact with pulmonary tuberculosis. Salivary glands never enlarged.

History.—Right pneumonia at the age of 9 years. Six years ago sudden onset of painful swelling and redness of both cheeks and nose. Radiotherapy in 1944; condition improved slightly. Soon after the face began to swell. Left index finger swollen and painful; amputated 22.3.45. Painful ulcer, soft palate, cleared up with sulphamezathine locally. In 1945 left great toe became painful and swollen; aching pain in shoulder, elbow-joints and back. Lassitude for the past three years. Cough for the past six years; brings up 1 oz. of non-offensive sputum; has never coughed blood.

The eyesight has been getting poor for the past six years. Mistiness and black moving spots. Eyeballs have never been sore. Right iritis and left cyclitis diagnosed 22.11.44.

On examination.—Fixed bluish induration over both cheeks and involving nose which is swollen and bulbous. Some scaling and dilated veins. Biopsy scar on each cheek. Patches of fixed purplish indurated erythema over lateral aspect of the arm. Some periarticular swelling of left wrist. Restriction of palmar flexion. Slight crepitus. Thickening and scaling of skin of palms; hands cyanosed. Swelling at proximal and intermediate phalanges of right middle finger, some limitation of movement. Not tender. Thickening and redness of patella. Swelling and purplish discoloration of right great toe. Scars of ulcers on legs (traumatic). Clubbing of fingers and toes. C.V.S.—N.A.D. Respiratory system: Medium moist crepitus which cleared on coughing heard at left mid-zone and right axilla. Some sibilant rhonchi at both bases.

Abdomen: Liver and spleen not palpable. Incisional hernia.

Right eye: Pupil small, edge blurred, irregular. Evidence of iritis. Reacts to light and constricts on convergence. Floaters in vitreous. Disc normal. **Left eye:** Pupil large, regular. Reacts to light and constricts on convergence. Floaters in vitreous. Some patchy haziness seen. Disc normal.

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Report on X-ray of chest: Mottled opacities in both lung fields with some linear markings in mid-zone, compatible with sarcoidosis, and ? some dilated bronchi on the left. There is a cystic area in the right mid-finger (middle phalanx) and also an alteration of cancellous structure of the terminal phalanx of the first toes of both feet. The appearances are those of sarcoidosis.

Sputum (3 specimens).—No acid alcohol-fast organisms seen.

Serum calcium.—9.5 mg. per 100 ml.

SEPT.—CLIN. 1

Fat analysis of the stools determined before, after the parenteral and after the oral treatment showed on the average little change (Table II).

TABLE II.—FÆCAL FAT EXCRETION IN CÆLIAC DISEASE

	Daily output in grammes	Total fat	Fat analysis, as a percentage of the dried faeces				No. of cases averaged
			Unsapon- ified	Sapon- ified	Free	Neutral	
Before treatment	6.12 (3.1-15.4)	40.1 (23.4-52.1)	30.3 (16.4-40.8)	10.8 (1.4-21.0)	20.8 (9.5-29.0)	9.5 (1.2-25.0)	22
After parenteral therapy	5.85 (1.8-14.3)	39.8 (17.4-50.0)	27.4 (8.7-40.0)	11.9 (7.5-18.0)	19.0 (8.4-28.5)	8.4 (0.3-15.5)	21
After oral therapy	6.0 (1.5-11.5)	38.7 (18.5-55.4)	25.2 (11.4-40.5)	13.8 (1.0-25.0)	15.1 (4.4-28.8)	9.9 (3.2-19.8)	17

The intravenous glucose tolerance curves were raised on admission approaching normal as treatment proceeded (fig. 1). The oral glucose tolerance curves showed little change, averaging a maximum rise of less than 40 mg. per 100 c.c. in the blood sugar (fig. 2). An improvement in the intravenous but not in the oral glucose curves suggested the effect of therapy was on the utilization of sugar rather than on its absorption. Nevertheless the persistence of a slight elevation of the blood pyruvic acid level indicated a continued disturbance of carbohydrate metabolism (Table III).

TABLE III.—BIOCHEMICAL AND HÆMATOLOGICAL FINDINGS IN CÆLIAC DISEASE.
(Average of 10 Cases.)

	Before treatment	After parenteral therapy	After oral therapy
Blood Pyruvic acid (mg.%)	1.12 (0.6-2.6)	1.30 (0.6-2.4)	1.38 (0.8-2.2)
Calcium (mg.%)	10.5 (8.3-11.5)	10.5 (9.6-12.4)	10.5 (9.0-13.0)
Phosphorus (mg.%)	4.6 (2.2-5.0)	4.8 (2.7-6.7)	5.1 (3.2-6.3)
Hb. (grammes%)	0.7 (7.4-12.4)	12.2 (8.0-13.0)	12.2 (8.0-13.0)
R.B.C. (millions)	4.62 (2.64-5.38)	4.54 (4.0-5.08)	4.54 (4.0-5.08)

The blood calcium and phosphorus averaged normal figures, though both tended to drop when the clinical condition deteriorated. In one case, not included in this series, values of 6.0 and 1.6 mg. per 100 c.c. respectively were obtained on more than one occasion in association with tetany. The presence of normal calcium and phosphorus levels did not guarantee the absence of osteoporosis and delay in ossification, though low levels were present in the more severe degrees of bone change (Table IV).

TABLE IV.—X-RAY CHANGES IN CÆLIAC DISEASE.

Before treatment	After treatment	No. of cases
Slight osteoporosis	Improved	2
Slight osteoporosis with slight rickets	Improved	1
Osteoporosis	Improved	3
Osteoporosis	Slightly improved	4
Osteoporosis	Not improved	5
Osteoporosis	Not improved with slight rickets	2

The hæmoglobin levels rose with treatment though transfusions were sometimes necessary in a crisis. In fact the blood as well as the whole clinical and metabolic picture was subject to considerable fluctuation. The rapidity with which the reception of the morning greeting would change from a smile to a frown reflected the lability of the patient's condition.

CONCLUSION

The administration of high doses of vitamin B and liver in cæliac disease ameliorates the strictness of the dietary treatment in the milder types. The more severe cases derive a less easily demonstrable benefit. From the data accumulated there is no evidence that this form of treatment is specific.

ACKNOWLEDGMENT

Thanks are due to Professor L. G. Parsons and Dr. E. M. Hickmans for their help in planning this study as well as for their criticism and advice.

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Plasma proteins.—Albumin 3.1 grammes, globulin 3.7 grammes, fibrinogen 0.39 grammes per 100 ml.

Blood-count.—Hb. 90% = 13.5 grammes%. Leucos. 10,300, neuos. 73%, lymphos. 20%, monos. 5%, cosinos. 2%.

Serum alkaline phosphatase 7.8 units; serum acid phosphatase 2.5 units.

Biopsy from cheek.—A heavily infected papillomatous lesion showing giant cells and endothelial cells. No tubercle bacilli seen. Appearances compatible with Boeck's sarcoid.

Mantoux 1 in 10,000 negative; 1 in 1,000 positive.

Dr. F. Parkes Weber emphasized the variety and striking character of the constituent features of this case of generalized Boeck-Schaumann sarcoidosis: (1) Hutchinson's "lupus-ernio" of the nose and rosaceous type of facial sarcoidosis; (2) indurated erythema of arm, &c.; (3) involvement of the respiratory system; (4) involvement of bones and bone-marrow, as in the cases so well demonstrated by Schaumann; (5) evidence of iritis and cyclitis, though without the parotid swelling of the so-called uveo-parotid syndrome (Heerfordt).

Dr. H. S. Stannus asked whether treatment by very large doses of calciferol as in lupus had ever been tried.

Dr. Herbert Levy said that arsenic and oleum morrhuate had been recommended for the treatment of sarcoidosis (the former by Snapper) but judgment of their effect is difficult as spontaneous recovery is so frequent. Kveim's report of a specific cutaneous reaction for sarcoidosis (A. Kveim, *Nord. Med.*, 1941, 9, 169; N. Danbolt and R. W. Nilssen, *Acta dermat. vener.*, 1945, 25, 489) where an extract from an involved lymph node is used as antigen would seem to deserve attention.

Lipodystrophy.—J. S. RICHARDSON, M.D. (Medical Unit, St. Thomas's Hospital).

E. Y., married woman, aged 53. Four children.

Normal and slim in appearance up to the age of 40, when she was ill for six months and had pleurisy with effusion. Immediately after this she noticed that her face was getting thinner, and one year later she began to put on weight over her hips and buttocks. Periods stopped two years ago, having been regular and normal from age of 13; still gets flushes; since 1942 has felt continuously tired with frontal headaches. Pain in legs, by day and night, for four months.

No family history of endocrine disorder or of abnormal fat distribution.

On examination.—Height 5 ft. Lower measurement 28½ in. Span 58¾ in. Abdomen lower costal margin 32 in. Buttocks at trochanters 47 in. Weight 11 st. 6 lb. Complete absence of subcutaneous fatty tissue over the face. Well-developed muscles of arms and shoulder girdles, which stand out owing to loss of subcutaneous fat. Skin normal without pigmentation. Breasts have lost almost all fatty tissue; lipoma at right anterior axillary fold. Abdomen covered by pendulous apron of fat; buttocks gross, irregular deposition of fat. Legs show pitting oedema with varicose veins and eczema. Muscle power, cutaneous sensation, skin and tendon reflexes normal. B.P. 120/80.

X-ray of chest and stereo X-ray of skull: N.A.D.

X-ray of lumbar spine shows marked osteoarthritis.

Urine: Sp. gr. 1022, acid—no abnormal constituents. 17-ketosteroids 7.6 mg. per 24 hours. B.M.R. minus 7. Blood: W.R. negative. Sugar (midday) 0.069%. Sugar tolerance curve normal. Calcium 8.2 mg., inorganic phosphate 3.1 mg., sodium 310 mg., chlorides 614 mg. per 100 c.c.

Blood-count.—R.B.C. 5,000,000; Hb. 100%; C.I. .99. W.B.C. 9,400 (polys. 49%, leucos. 34%, monos. 10%, basos. 1%, cosinos. 6%).

Fat tolerance test (G. Popják).—Plasma lipids (mg./100 ml.) before and after ingestion of 80 grammes of butter fat. Test performed fifteen hours after the last meal.

Time after fatty meal hour	Non-phospho-lipid fatty acids	Neutral fat	Phospho-lipid	Cholesterol	Total
0	301	266	280	Free 58 Ester 190	248
1½	386	267	280	57	239
3½	549	429	298	61	255
5½	655	537	308	66	265
8½	615	495	322	66	265

Dr. F. Parkes Weber said that a feature in the present case was the relatively late onset of the symptoms—nearer to the climacteric period than to the onset of puberty. The excessive accumulation of subcutaneous fat in the lower part of the trunk and thighs approached the type specially described by Laignel-Lavastine and Viard; it did not occur in most of the rare cases in males. Altogether, one might liken typical "lipodystrophia progressiva" in females to a caricature of the change which normally takes place in many middle-aged women when they "spread out" in the lower part of the trunk and get thinner in the face (cf. F. P. Weber, *Lipodystrophia Progressiva*, London, 1918, pp. 10–12).

[May 10, 1946]

Case for Diagnosis. ? Congenital Heart Disease with Atrial Septal Defect: ? Mitral Stenosis.
—COURTENAY EVANS, M.D.

Miss G. C., aged 43.

History.—Tired and short of breath. Heart found to be enlarged and abnormal a year ago. No rheumatic fever or illnesses in childhood.

On examination.—Heart enlarged. Rhythm regular. No congestive failure. Apex beat in sixth space, just outside mid-clavicular line. Loud systolic murmur at apex, conducted outwards. First sound loud, slight suggestion of presystolic murmur. Systolic murmur also heard over second and third interspaces (left). B.P. 140/90.

X-ray examination.—Heart: Considerable enlargement of pulmonary artery and its branches, pulsation in right and left pulmonary artery branches. Right ventricle enlarged. Barium swallow does not show any dilatation of left auricle. Electrocardiogram: Right axis deviation with widening of Q.R.S. to 0.08 sec. T wave inversion in lead 3 and also in chest lead C.R.I. Early right bundle branch block.

W.R. negative.

Dr. A. Schott agreed that this was a case of interauricular septal defect with mitral stenosis, i.e. Lutembacher's syndrome. Mitral valvular disease alone could be excluded, as in that case the patient would have been far more seriously ill; moreover, enlargement of the left auricle, for which there was no radiological evidence in this case, would have to be expected, whereas such enlargement is frequently absent in patients in whom mitral stenosis is associated with interauricular septal defect. Eisenmenger's syndrome, i.e. interventricular septal defect, right-sided enlargement, dextroposition of the aorta and dilatation of the pulmonary artery was unlikely as this condition is very rare as compared with the relative frequency of Lutembacher's syndrome and cyanosis seems to be more marked and to occur earlier in Eisenmenger's syndrome than was observed in this case.

Idiopathic dilatation of the pulmonary artery cannot be differentiated radiologically from interauricular septal defect, but its association with mitral stenosis has not been observed; moreover, this condition also is very rare as compared with Lutembacher's syndrome.

Cirrhosis and Ascites (Treated by Omentopexy Twelve Years ago after Investigation by Thorium Dioxide).—ARTHUR E. PORRITT, C.B.E., F.R.C.S.

Mrs. E. L., aged 69.

First referred to St. Mary's Hospital in October 1934 having previously attended another hospital since July of that year. She was originally diagnosed as a large ovarian cyst. Laparotomy (August 1934) showed nothing abnormal in the pelvis, a marked liver enlargement and massive ascites—2½ gals. of fluid being aspirated on this occasion. The hepatic masses chiefly in the left lobe were described as "lobular rather than nodular and not umbilicated". No primary growth was discovered.

In October 1934 ascites was again found and on admission the umbilicus was everted by distension, and shifting dullness and a fluid thrill were present. Temperature, pulse and respiration were normal, but the urine contained blood and pus and a well-marked uterine prolapse was present. The patient had had three healthy children and a straightforward menopause eight years previously.

The abdomen was tapped, 5 pints of pale yellow fluid being removed which did not clot on standing, contained 800 cells per c.c., chiefly endothelial and lymphocytes.

75 c.c. of "thorotrast" (thorium dioxide) were injected intravenously in 3 doses of 25 c.c., a two-day interval being left between each injection. Reactions were minimal and two days later a good picture of the liver and spleen was taken, the shadow of the latter being considerably denser (Dr. Gage and Dr. Rohan Williams). Appearances suggested cirrhosis and the presence of a Reidel's lobe.

A week later a mid-line supra-umbilical laparotomy was performed, the peritoneal surfaces of liver and spleen roughened to oozing point with dry gauze and the omentum brought through and implanted in the layers of the anterior abdominal wall (Talma Morrison operation).

The blood picture was: R.B.C. 4,800,000; Hb 88%; C.I. 0.9. W.B.C. 5,500.

Two weeks later, 7 pints were aspirated from the abdomen and the patient was discharged one month after the omentopexy. One month later, 4 pints of ascitic fluid were removed.

She was kept under frequent observation until June 1939. At no time did the hæmoglobin fall below 72%, the R.B.C. below 4,350,000 and the W.B.C. below 5,000.

Plasma proteins.—Albumin 3.1 grammes, globulin 3.7 grammes, fibrinogen 0.39 grammes per 100 ml.

Blood-count.—Hb. 90% = 13.5 grammes%. Leucos. 10,300, neuros. 73%, lymphos. 20%, monos. 5%, eosinos. 2%.

Serum alkaline phosphatase 7.8 units; serum acid phosphatase 2.5 units.

Biopsy from cheek.—A heavily infected papillomatous lesion showing giant cells and endothelial cells. No tubercle bacilli seen. Appearances compatible with Boeck's sarcoid.

Mantoux 1 in 10,000 negative; 1 in 1,000 positive.

Dr. F. Parkes Weber emphasized the variety and striking character of the constituent features of this case of generalized Boeck-Schaumann sarcoidosis: (1) Hutchinson's "lupus- pernio" of the nose and rosaceous type of facial sarcoidosis; (2) indurated erythema of arm, &c.; (3) involvement of the respiratory system; (4) involvement of bones and bone-marrow, as in the cases so well demonstrated by Schaumann; (5) evidence of iritis and cyclitis, though without the parotid swelling of the so-called uveo-parotid syndrome (Heerfordt).

Dr. H. S. Stannus asked whether treatment by very large doses of calciferol as in lupus had ever been tried.

Dr. Herbert Levy said that arsenic and oleum morrhuate had been recommended for the treatment of sarcoidosis (the former by Snapper) but judgment of their effect is difficult as spontaneous recovery is so frequent. Kveim's report of a specific cutaneous reaction for sarcoidosis (A. Kveim, *Nord. Med.*, 1941, 9, 169; N. Danbolt and R. W. Nilssen, *Acta dermat. vener.*, 1945, 25, 489) where an extract from an involved lymph node is used as antigen would seem to deserve attention.

Lipodystrophy.—J. S. RICHARDSON, M.D. (Medical Unit, St. Thomas's Hospital).

E. Y., married woman, aged 53. Four children.

Normal and slim in appearance up to the age of 40, when she was ill for six months and had pleurisy with effusion. Immediately after this she noticed that her face was getting thinner, and one year later she began to put on weight over her hips and buttocks. Periods stopped two years ago, having been regular and normal from age of 13; still gets flushes; since 1942 has felt continuously tired with frontal headaches. Pain in legs, by day and night, for four months.

No family history of endocrine disorder or of abnormal fat distribution.

On examination.—Height 5 ft. Lower measurement 28½ in. Span 58¾ in. Abdomen lower costal margin 32 in. Buttocks at trochanters 47 in. Weight 11 st. 6 lb. Complete absence of subcutaneous fatty tissue over the face. Well-developed muscles of arms and shoulder girdles, which stand out owing to loss of subcutaneous fat. Skin normal without pigmentation. Breasts have lost almost all fatty tissue; lipoma at right anterior axillary fold. Abdomen covered by pendulous apron of fat; buttocks gross, irregular deposition of fat. Legs show pitting œdema with varicose veins and eczema. Muscle power, cutaneous sensation, skin and tendon reflexes normal. B.P. 120/80.

X-ray of chest and stereo X-ray of skull: N.A.D.

X-ray of lumbar spine shows marked osteoarthritis.

Urine: Sp. gr. 1022, acid—no abnormal constituents. 17-ketosteroids 7.6 mg. per 24 hours. B.M.R. minus 7. Blood: W.R. negative. Sugar (midday) 0.069%. Sugar tolerance curve normal. Calcium 8.2 mg., inorganic phosphate 3.1 mg., sodium 310 mg., chlorides 614 mg. per 100 c.c.

Blood-count.—R.B.C. 5,000,000; Hb. 100%; C.I. .99. W.B.C. 9,400 (polys. 49%, leucos. 34%, monos. 10%, basos. 1%, eosinos. 6%).

Fat tolerance test (G. Popják).—Plasma lipids (mg./100 ml.) before and after ingestion of 80 grammes of butter fat. Test performed fifteen hours after the last meal.

Time after fatty meal hour	Non-phospho- lipid fatty acids	Neutral fat	Phospho- lipid	Cholesterol		Total
				Free	Eester	
0	391	266	289	58	190	248
1½	386	267	280	57	182	239
3½	549	429	298	61	194	255
5½	655	537	308	66	199	265
8½	615	495	322	66	199	265

Dr. F. Parkes Weber said that a feature in the present case was the relatively late onset of the symptoms—nearer to the climacteric period than to the onset of puberty. The excessive accumulation of subcutaneous fat in the lower part of the trunk and thighs approached the type specially described by Laignel-Lavastine and Viard; it did not occur in most of the rare cases in males. Altogether, one might liken typical "lipodystrophia progressiva" in females to a caricature of the change which normally takes place in many middle-aged women when they "spread out" in the lower part of the trunk and get thinner in the face (cf. F. P. Weber, *Lipodystrophia Progressiva*, London, 1918, pp. 10–12).

of constant iron treatment a count on April 30 showed: R.B.C. 4,010,000; Hb. 68%. Intermittently, there was sinus formation to the skin over the horizontal ramus of the right mandible.

Comment.—"Pellagra is certainly a rare disease in Great Britain" (H. S. Stannus and C. R. Gibson, 1934, *Quart. J. Med.*, N.S. 20, 211): the second World War has not made it less rare in Great Britain. Working for the greater part of the war in hospitals serving particularly poor districts of London where at least 4 to 5 cases of frank scurvy came under my charge per year, I saw two cases of an acute hallucinatory psychosis in elderly afebrile patients who lost their psychotic symptoms within twenty-four to forty-eight hours of parenteral nicotinamide treatment (cf. B. Gottlieb, 1944, *Brit. med. J.* (i), 392) but neither of them had any skin lesions. This patient is the first I have seen during that time showing the full picture of pellagra. Unfortunately, it was not possible to obtain a reliable dietary history, but undoubtedly the carcinoma of the mouth from which he suffered in 1944 and 1945 will have changed his dietary habits. The skin lesions included areas which had never been exposed to sunlight.

Dr. H. S. Stannus: Dr. Levy's case of pellagra illustrates very well so many of the symptoms met with in that disease and at the same time serves as a basis for discussion of some of the fallacious observations often made concerning the signs and symptoms which may occur. It is only possible to refer to a few points.

The extension of the dermatitis to the dorsa of the toes is well shown. It would be interesting to learn whether the toes had been exposed to sunshine preceding the appearance of the exanthem. The fact is, as I first pointed out many years ago, that the dermal manifestations tend to appear in any area of skin in which as the result of past trauma of any kind, including equally sunshine and chapping due to cold, the capillaries have suffered permanent damage. The almost universal extension of the dermatitis to the flexor aspects of the wrists also seen in this case can only thus be explained.

The oil-silk or lacquered appearance of the skin of the shins in this man is a condition rather characteristic of chronic pellagra. It sometimes shows cracking, giving a condition often referred to as "crazy-pavement" skin.

I will only refer to one other point—diarrhoea; this is by no means a constant symptom as has often been asserted, in many cases constipation is present. And a word of warning—the administration of a purge may then set up an intractable diarrhoea. In regard to treatment by nicotinic acid, I think it might be advisable to give large doses, 500 mg. per day in divided doses of 100 mg. each.

Hypertension treated by Arteriovenous Anastomosis.—A. DICKSON WRIGHT, M.S., F.R.C.S.

G. B., aged 40, seen in February 1946 with advanced malignant hypertension. His systolic blood-pressure varied from 250-300 and diastolic from 150-170. His main symptoms were bad nightmares, claudication in the legs and rapid deterioration of vision.

On examination.—There was extensive retinal damage from hæmorrhage and exudation and papilloedema. Pulsus alternans was present with 50 mm. difference between alternate pulses. The blood urea was 120 mg. per 100 c.c. and urine contained much albumen. Anastomosis between the left external carotid and external jugular was made on February 26, and two weeks later his blood-pressure was 175/115.

On March 29 he reported himself as "feeling better than for a long time". His complexion and aspect were better and he was sleeping well and could read the paper, and although he could hear the murmur it did not keep him awake. The pulsus alternans was still present with 10 mm. difference between beats and his blood-pressure was 210/115. The blood urea was now only 32 mg. and albumen was only slight. On closing the fistula with finger pressure the systolic rose 40, the diastolic pressure 50 points. The operation was done to provide a safety valve to preserve the vision in a hopeless case of hypertension, the improvements in other directions were unexpected and would repay investigation.

Lymphadenoma.—By LEO RAU, M.D., M.R.C.P.

Female, aged 24. Was first seen in May 1941, after she had been ill for six months. Her complaints were backache, vomiting without any reason or warning, hoarseness, loss of weight from 10 st. 7 lb. to 8 st. Her periods had always been normal. On examination—typical right Horner's syndrome, palsy of right recurrent nerve, typical lymph glands in right neck. Spleen and liver not palpable. Diagnosis: Lymphadenoma.

Investigations.—Secondary anæmia, marked anisocytosis and microcytosis. Differential leucocyte count: Polys. 83%, lymphos. 7%, monos. 9% and eosinos. 1%. Radiograph of chest—large shadows in both mediastina, typical of Hodgkin's disease (see fig. 1).

Dr. F. M. Allchin, at Westminster Hospital, undertook treatment. Between May 1941 and June 1944 she received six courses of deep X-ray therapy as an out-patient. The first

She was not seen again until March 1946—eleven and a half years after the omentopexy and the injection of thorotrast. No tapping had been done since the two immediate post-operative ones described above. She was in excellent health and had been so throughout the period. Her blood examination now showed Hb. of 76% and R.B.C. count of 4,500,000. An X-ray examination had not yet been possible. A W.R. taken during the war was ++, and the Kahn +++, but it should be noted that no anti-specific therapy has been given at any time.

The interest of the case lies in the completely successful result of an omentopexy for the ascites and what is presumably a specific cirrhosis and in the fact that a very enlarged liver and spleen filled with thorium dioxide for practically twelve years has to date given no ill-effects either on the blood picture or elsewhere.

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James J., aged 70.

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Admitted Bethnal Green Hospital March 31, 1946, on account of pain in right posterior chest wall following a fall the previous day.

On examination.—Lying perfectly listless with dull lifeless stare, continuously rubbing his face and hands. Answers question as to site of pain only after considerable delay; does not answer any other simple questions.

Dermatitis of face and part of neck with considerable infiltration of skin, the colour being nearly that of an erysipelas. Chronic dermatitis with lichenification of back of hands and distal forearms. Alligator-like hyperkeratosis of skin (dark brown-blackish) over back of feet and toes up to distal fourth of legs; the hyperkeratotic tissue can be fairly easily separated from the underlying dermis, leaving a raw surface. Patch of chronic dermatitis at inner side of left thigh. Pigmentary marmoration *ab igne* over parts of lower limbs. (The skin lesions had been noticed by his wife for "some months" and the facial eruption had some four months ago been diagnosed, and treated, as erysipelas.) Scratch-marks on forearms and legs with areas of secondary infection.

Marked pallor of visible mucous membranes but no other abnormalities of oral mucous membrane, angles of mouth, tongue, or anal sphincter. Small patches of pigmentation on inner and outer parts of bulbar conjunctivæ; no circumcorneal injection to naked-eye inspection.

Gross defect of right mandible with localized dimpling of soft tissues but no sinus opening. No significant lymph-node enlargement at neck. No reduction in amount of subcutaneous fat. Muscle tone within normal limits for age-group. Deep and plantar reflexes normal. Localized tenderness over seventh right rib in mid-scapular line. Liver reaches to 1 in. below costal margin. No other relevant findings.

Blood examination (Dr. J. M. Alston).—3.4.46: R.B.C. 3,740,000; Hb. 66%. W.B.C. 6,900 (neutr. polys. 70%, eosino. polys. 4%, lymphos. 26%).

10.4.46: Skiagrams; No evidence of metastases in pelvis or ribs; right lower jaw shows large area of destruction with fracture.

15.4.46: Serum albumin: 3.9 grammes %; serum globulin 3.6 grammes %; serum Ca: 11 mg.%; inorganic P. 4.5 mg.%; acid phosphatase: 1.7, and alkaline phosphatase 9 units.

6.5.46: Fractional test meal: Normal acidity.

Treatment with nicotinamide, crude liver extract, marmite, and ferrous sulphate was started on admission (nicotinamide 300 mg. on first day, 200 mg. daily on next two, and 150 mg. on following ten days subcutaneously). The angry redness and a good deal of the inflammatory infiltration of the facial eruption disappeared within forty-eight hours; the hyperkeratotic crust on the feet had entirely peeled off after about three weeks, leaving a skin with fairly sharply limited hyperpigmentation and some lichenification as visible still now, five weeks after admission.

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Repeated blood-counts never revealed any abnormality with the exception of a hypochromic anæmia and lymphopenia.

With the X-ray treatment she has been kept sufficiently fit to carry on her work efficiently. She is one of the few instances of this unpleasant disease that has benefited by radiation therapy.

Jejuno-gastric Intussusception.—W. H. J. WESTON, F.R.C.S., introduced by Ivor LEWIS, M.S.

R. C., male, aged 43, milk roundsman, admitted to the North Middlesex County Hospital March 27, 1946, after two and a half days of violent abdominal pain. The pain woke him and immediately he vomited clear yellow fluid. Eighteen years previously he had had a gastrojejunostomy performed.

The pain began in the left hypochondrium and was said to be a "steady" pain. After the pain had begun he passed neither fæces nor flatus. He was a thin man with sunken eyes, a dry tongue, and washerwoman's fingers. The vomit was reddish-brown.

A vague tender mass could be felt in the left hypochondrium and the iliac fossæ were curiously empty. Violent peristaltic sounds could be heard.

A diagnosis of high intestinal obstruction was made, almost certainly due to stoma intussusception. An upright X-ray of the abdomen showed, not the large gas-dilated fundus of stomach and fluid levels of other acute intestinal obstruction cases, but a stomach filled by a mass of intussuscepted gut.

At operation (Mr. Ivor Lewis) an intussusception of the efferent limb of the gastrojejunostomy into the stomach was found. The loop was reduced by pressure from above and gentle traction.

After three days' continuous gastric aspiration and intravenous fluids he made a good recovery.

One month after operation a barium meal showed a normally functioning gastrojejunostomy.

Hand-Schüller-Christian Syndrome.—M. B. MATTHEWS, M.B., M.R.C.P.

H. R., an insurance agent, aged 47, was referred by Dr. Smiles of Wokingham to St. Thomas's Hospital in May 1946 with a diagnosis of Hand-Schüller-Christian syndrome. His chief complaint was dizziness for one month. There was nothing relevant in his past history before 1928. He stated that his maternal grandfather had died of the "drinking diabetes".

In 1928 he first noticed that he had "lost his saliva"; since then his mouth has been persistently dry and he has been accustomed to eat fruit with bread and butter so as to make mastication easier. There has been no polyuria. In 1933 all his teeth were extracted for pyorrhœa and for the following four years he wore dentures. In 1936 he first noticed a swelling on the tip of the mandible. This made his dentures uncomfortable and early in 1937 he attended the Royal Berkshire Hospital, Reading, where an X-ray showed a cavity in the mandible. Histological examination of the tissue obtained from this cavity showed "large spheroidal cells with oval nuclei, infiltrated with a large number of wandering cells, mainly polymorphs". The pathologist was not prepared to say whether the process was neoplastic. In 1936 an ulcer of the rectum which was thought clinically to be tuberculosis was excised locally; histological examination showed no evidence of tuberculosis. In 1938 his wife first noticed that the patient had exophthalmos. Also in this year he had persistent root pains at about the level of D.6 worse in the morning, better on movement and relieved by aspirin four-hourly. After six months the pain gradually improved. The mandible was irradiated in this year as small pieces of bone were discharging into the mouth. After six months the discharge ceased but the mandible has become progressively smaller. Coincidentally a swelling about the size of a walnut appeared in the skin over the right maxilla. There is no report available about this, but it disappeared following deep X-ray therapy. For the last three years he has noticed that his enunciation has become difficult. Since then, until recently, his only symptoms have been a non-productive cough, lassitude and persistent dryness of the mouth.

In April of this year he first noticed dizziness and deafness of the left ear, without true vertigo, making walking difficult. He still has slight dizziness in the morning. There are no other abnormal symptoms and he has lost no weight.

On examination.—Normally-developed adult male, weighing 128¾ lb. Marked bilateral exophthalmos with limitation of ocular movements in all directions. The mandible is very wasted, producing a shrew mouse profile; the soft tissues are preserved. There is no anæmia or lymphatic glandular enlargement. Apart from slight slow nystagmus to the

treatment was to the chest, which received 3,600 r. After this, the Horner's syndrome and the paralysis of the recurrent nerve disappeared. She remained well until November 1942, and in December 1942 the left supraclavicular and left axilla were treated by deep X-ray therapy. Each area received 1,000 r. She remained well until July 1943 when enlarged glands on the left side of her neck were treated, and a dose of 1,800 r was given. In October 1943, she complained of pain in the chest. Radiographs showed congestion of the right base, and some irregular shadows just below the interlobar line. She was given a further course of deep X-ray therapy, 3,400 r skin dose to the chest. She remained well, but in March 1944 there was infiltration of both bases, and a further skin dose of 2,200 r was given to the chest. In June 1944, glands of the left axilla became enlarged and 2,000 r were given. In January 1945 she complained of some pain in the right side of the chest and pyrexia. There was loss of weight. A further course of deep X-ray therapy, 2,000 r to the anterior superior mediastinum and again 2,700 r to the left base was given. In June 1945 she reported feeling very weak, was unable to walk and there was a mass in the abdomen. She was treated through one port, 10 x 8 cm. and a skin dose of 1,500 r was given. She improved rapidly and remained well until December 1945. She developed a troublesome cough, pain in the left side of the abdomen. X-rays showed no obvious glandular enlargement but extensive bilateral pulmonary involvement. 3.1.46: Hb. 66%; W.B.C. 11,600 (polys. 9,744 per c.mm., lymphos. 812 per c.mm.). She improved rapidly following deep X-ray therapy, 1,200 r anteriorly, and 1,300 r posteriorly to the right mid-zone of the chest. She has remained well since then.

For the last fifteen months she has been working as a cashier in one of the big stores and feels fit. Her weight (May 1946) is 7 st. 6½ lb. She looks well. Spleen and liver are not palpable. There are a few glands palpable in the left side of the neck and left groin, supra-inguinal. The X-ray of the chest shows no obvious glandular enlargement but some pulmonary involvement: right pulmonary infiltration and collapse of left lower lobe.

Comment.—Although there has been no biopsy of a gland, there cannot be much doubt that this is a case of lymphadenoma. Clinically, the recurrences of palpable glands in the different regions and the original radiogram of the chest are typical of the disease. The X-ray appearances of the chest during the five years may not be specific, but the disappearance of the manifestations after X-ray treatment is, I believe, typical of the disease. The follow-up of the radiographs of the chest is most instructive, as at times the films reveal pathology which might be explained as areas of collapse due to regional lymphadenomatous lymphangitis, and others show larger nodules infiltrating the lung tissue.

Without the follow-up many of the radiographs show pathology which could be mistaken for pulmonary tuberculosis, or Boeck's sarcoid, or Loeffler's syndrome, such as has been shown by Elkeles and others in this Section. [See figs. 1 and 2.]

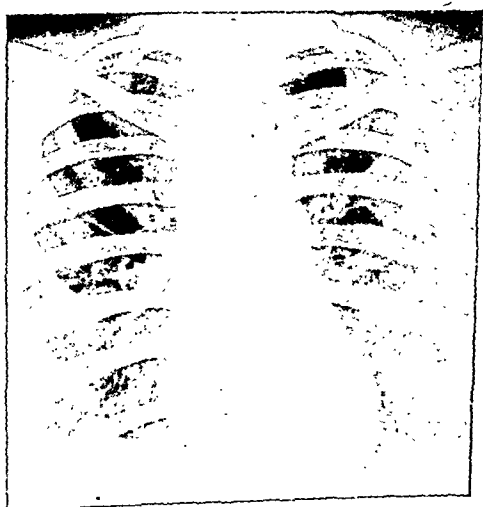


FIG. 1. 9.6.41.
Enlargement of mediastinal glands.

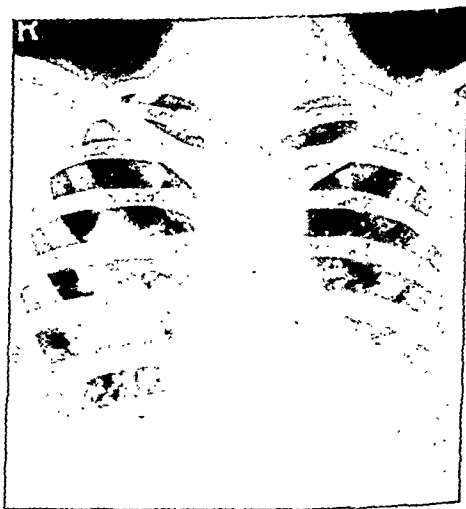


FIG. 2. 30.5.45.
Infiltration of right mid-zone and hilar glands; further
bilateral infiltration of lower lobes.

Section of Orthopædics

President—W. B. FOLEY, F.R.C.S.

[May 21, 1946]

A Method of Treating Bennett's Fracture

By V. H. ELLIS, F.R.C.S.

BENNETT'S fracture, dislocation of the first metacarpal, is a comparatively common injury. A bad anatomical result of treatment gives a bad functional end result. Reduction is not difficult as a rule, but the maintenance of position is the chief problem. The usual method of fixation advocated is by traction on the thumb with joints extended, together with plaster fixation with close moulding round the base of the metacarpal.

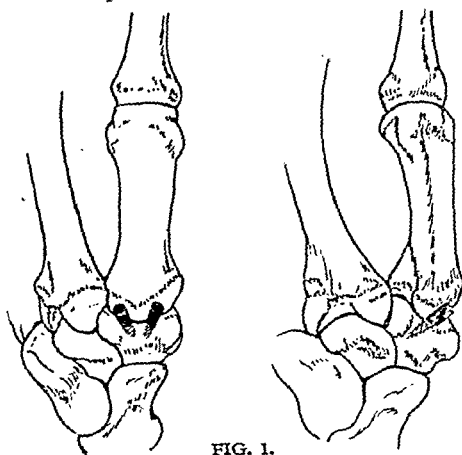


FIG. 1.

The method I have devised involves the exposure of the outer aspect of the carpo-metacarpal joint, reduction of the fracture and its maintenance in position by two short pegs or nails introduced obliquely into the trapezium forming a shelf so that redislocation cannot occur (fig. 1). The pegs are inserted in drill holes about one-third of an inch deep and project sufficiently to support the base of the metacarpal. The skin is sutured over the pegs and the thumb and wrist immobilized in a scaphoid type of plaster which allows good use of the hand. Immobilization is continued for six weeks. Then the plaster is removed and the pegs taken out at a further minor operation.

The five-year results in two cases are very good, and in six or seven others there is no reason to expect any permanent disability.

A Method of Treating Fractures of the Neck of the Talus

By V. H. ELLIS, F.R.C.S.

Fracture of the neck of the talar bone with displacement is usually associated with subtaloid dislocation. I am not concerned with the variety in which the body of the talus is displaced backwards out of the ankle mortice.

Reduction of fracture of the neck of the talus is usually easy by manipulation into full plantar flexion and eversion. The usual practice is to immobilize the limb in this position.

The surgeon is now in a dilemma. Prolonged immobilization in full equinus may lead to a fixed deformity. Placing the foot at a right angle too early causes redisplacement of the fracture.

In my experience a fixed equinus may develop in seven to eight weeks, especially in older patients. I have overcome this difficulty by introducing a quarter-inch graft from the tibia into the long axis of the talus from behind, after reduction has been achieved by manipulation. This fixes the fracture sufficiently to allow immediate immobilization of the ankle at 90 degrees.

With the patient prone and the knee flexed a graft of $4\frac{1}{2}$ cm. long and quarter of an inch wide is taken from the tibia. The knee is now extended and the fracture reduced by manipulation.

right there are no abnormal signs in the central nervous-system. Air entry is diminished at the left apex with post-tussic crepitations at the right base. The cardiovascular system is normal; the blood-pressure 140/90. There are no abnormalities in the gastro-intestinal tract. The urine contained a trace of albumin on one occasion but no Bence-Jones proteose. Apart from wax in the left ear, no abnormality could be found in the ears, nose or throat. There is a marked kyphosis of the level of about C.7. There is no bone tenderness in the spine, nor palpable abnormality in the skull or long bones. There are two small yellow intracutaneous plaques on the outer sides of each eye, considered by Dr. Dowling to be xanthomata.

Investigations.—

	Fasting plasma lipids	mg. 100/ml.	Serum calcium	10 mg.%
Non-phospholipid fatty acids	232	Inorganic phosphate	4 mg.%
Neutral fat	126	Alkaline phosphatase	4 units
Phospholipids	222	Blood-count.—	
Free cholesterol	55	R.B.C.	5,500,000 per c.mm.
Ester cholesterol	155	Hb.	68%
Total cholesterol	210	C.I.	0.6
			Leucocytes	21,000 per c.mm.
			(polys. 87%, lymphos. 4%, monos. 7%, eosinos. 2%).	

Sternal marrow normal. Blood Wassermann reaction negative. Blood sedimentation rate—49 mm. in 1 hour.

Glucose Tolerance Test (50 oz. glucose orally 9.30 a.m.)

Time hrs.	Blood sugar mg.%	Urine sugar
0	150	
1	160	
1½	192	
2	209	Nil
2½	213	
3	228	Nil
	203	Nil

Radiographs.—In the skull there are extensive changes of xanthomatosis throughout with involvement of left mastoid, right maxilla and whole mandible. The orbital fissures are not distinguishable. The spine shows collapse of D.6. There is a uniformly dilated uncoiled aortic arch with reticulation of both lung fields, chiefly of the lower lobes. In the pelvis there are extensive changes with rarefaction and sclerosis. The right femur shows bone sclerosis and thickening of periosteum. The appearance is similar to that of Paget's disease. The left and right radii show areas of slight rarefaction.

While in hospital he has run a slight intermittent fever up to 99.6°. The specific gravity of the urine varies between 1010 and 1015; the daily output is normal.

The patient was unwilling to undergo plastic reconstruction of the jaw. As he was anxious for the proptosis to be reduced a course of X-ray therapy directed at the retro-orbital area was given. Although no measurements with the proptometer were made, there was objective and subjective improvement. A total of 2,000 r was given, over a period of ten days: 200 r for seven days, then 100 r, 250 r and 250 r on successive days.

SUMMARY

A case of Hand-Schüller-Christian syndrome of at least six years' duration in a man aged 47 is described. There was exophthalmos and wasting of the mandible, extensive and typical bone change but no diabetes insipidus and the blood cholesterol was normal.

My thanks are due to Professor de Wesselow, under whose care the patient was, for permission to publish the details of this case.

clinically evident and those that are silent, make it important to adopt any form of treatment which by raising the patient's resistance will have a general effect. The value of constitutional treatment in this respect is recognized. The effect of operation on raising resistance should also be considered.

I have formed an impression that benefit is gained in many cases by operation and that such benefit is not only local but general. Operation might raise resistance either by removing a source of tuberculous toxæmia, or by liberating into the tissues tuberculous inflammatory products which might act as specific antigens. Such a process might account for the beneficial effect of laparotomy in tuberculous peritonitis. Two observations may be quoted in favour of there being some benefit due to auto-inoculation. The first is the marked improvement in the general condition which may follow operation on tuberculous bone. This observation has been noted by others, notably Lavalley and McCrae Aitken. Certainly it has been confirmed in my experience. The effect may follow simple osteotomy through tuberculous bone without the removal of any tuberculous tissue. The second observation is the poor result which so frequently follows treatment of a tuberculous joint by amputation of the limb. Of 10 cases which had had an amputation only 3 remained permanently well. 3 died and 4 developed tuberculous lesions in other parts of the body.

I therefore examined the records of 129 patients admitted to Black Notley during the past ten years; these patients had skeletal tuberculosis complicated by associated tuberculous lesions, either in other parts of the skeleton, in the lungs, the genito-urinary system or the salpinges. These patients were divided into two groups, one of 49 cases who had had any operation into tuberculous tissue from which an auto-inoculation effect might have been obtained, and the other of 80 cases who had had no such operation. In assessing the results it appeared that some of the patients in the non-operated group might have been patients who were too advanced for operation and that this would spoil the two groups for the purpose of comparison. Therefore I subdivided the cases in both operated and non-operated groups into cases of moderate severity and marked severity, and the results into three groups, good, moderate and poor.

It was found that the percentage of cases of those who did well was quite high in both groups, 73·5% in the operated group and 66·3% in the non-operated group. This would be expected in any series of tuberculous patients treated thoroughly by constitutional measures and splintage. In the operated group 14·3% had moderate results, in the non-operated group 8·7%; there were poor results in 8·2% of the operated group and in 7·5% of the non-operated. Deaths in the operated group were 4%, in the non-operated 17·5%. Yet the percentage of cases of marked severity in the operated group was 28·5%, in the non-operated group 17·5%. So that the operated group was not a favoured group: yet the results were better in this group.

Though these figures may not be statistically significant they do tend to support the other evidence. It appears that especially in the desperate cases operation may carry benefit. There is no valid reason for withholding operation from patients with multiple tuberculous lesions, and their prognosis is better with operation than without. There is reason to believe that this may be due to an auto-inoculation effect.

No patient developed a permanent sinus following operation. Operation should not be done until a fair degree of resistance has been established, or miliary tuberculosis may supervene.

The Treatment of the Uncorrected Clubfoot in Childhood

By J. S. BATCHELOR, F.R.C.S.

I PROPOSE to describe a method of treatment that I have found useful for uncorrected, or imperfectly corrected, clubfeet in young school children: that is, in children from the age of 5 years to 10 or 12, when they are old enough to have a formal arthrodesis done if this should be necessary.

I have been much impressed by the disability that the uncorrected clubfoot produces in children in this age-group, for many of them are greatly handicapped in walking and have considerable difficulty with footwear. Moreover, they are frequently subjected to repeated manipulations, wrenchings and plaster immobilization of their deformed feet.

The results of this conservative treatment cannot be considered satisfactory. Manipulative trauma tends to produce a vicious circle of false correction, increasing fibrosis

The foot is held plantar-flexed and everted, and the position checked by X-ray. The posterior aspect of the talus is now exposed by vertical incision lateral to the tendo achillis (fig. 2).

The point of a Hey-Groves director is applied to the medial side of the head of the talus, and a guide wire introduced immediately above the ridge separating the ankle from the subtalar joint. The guide is introduced $4\frac{1}{2}$ cm. and a check X-ray taken.

The guide wire is now withdrawn and the track enlarged with drills until the graft can be hammered home. The graft lies above and parallel to the subtalar joint and in the long axis of the bone (fig. 3).

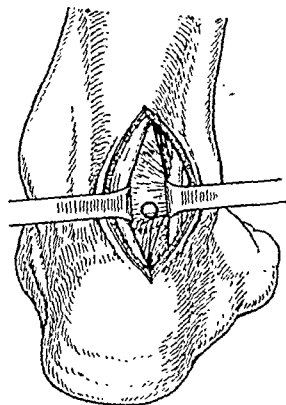


FIG. 2.



FIG. 3.



FIG. 4.

The wound is now closed and the foot can be safely dorsiflexed to a right angle. It is plastered in this position.

The anatomical and functional results in three cases have been excellent, and at five months there is no evidence of avascular necrosis of the body of the talus (fig. 4).

The Treatment of Bone Tuberculosis in Relation to Multiple Tuberculous Lesions

By M. C. WILKINSON, M.B.

MULTIPLICITY of tuberculous lesions undoubtedly makes the prognosis of tuberculosis worse: in this respect associated lesions in the skeleton are of only slight consequence, associated lesions in the genito-urinary tract are of more significance, and associated pulmonary tuberculous lesions may be the most grave. Nevertheless complete recovery can occur in spite of multiple lesions.

In discussing tuberculous lesions associated with bone tuberculosis I would distinguish between tuberculosis of the lymphatic glands, which I believe exercise a barrier effect against invasion of the blood-stream, and hæmatogenous tuberculous foci. The two types do not usually exist together. If there is a heavy glandular infection this is evidence of good resistance of the lymphatic tissues; if there are multiple hæmatogenous lesions, I think that the lymphatic tissues at the portal of entry have been inadequate. Similarly a good relative lymphocytosis is evidence of activity of the lymphatic defence and is of good prognostic import. As the lymphatic tissues reach their peak of activity during childhood, and wane gradually after adolescence, it is not surprising to find that the majority of childhood lesions are in the lymphatic glands, that skeletal lesions occur only in a minority of infected children, that multiple lesions tend to occur more frequently after adolescence, and that the incidence of multiple lesions increases as age advances. As a corollary it follows that when a patient has both a skeletal lesion and associated gross tuberculous lymphadenitis the prognosis for the skeletal lesion is usually very good, as the patient's resistance is high. With regard to associated lesions other than in the lymphatic system, the incidence in a series of 340 cases of skeletal tuberculosis was 25.3%. Nevertheless this must be a gross understatement of the incidence of such lesions as with improved methods of diagnosis it is easier to detect silent lesions, often present, and previously only suspected. The wide distribution in the body of hæmatogenous tuberculous lesions, both those that are

clinically evident and those that are silent, make it important to adopt any form of treatment which by raising the patient's resistance will have a general effect. The value of constitutional treatment in this respect is recognized. The effect of operation on raising resistance should also be considered.

I have formed an impression that benefit is gained in many cases by operation and that such benefit is not only local but general. Operation might raise resistance either by removing a source of tuberculous toxæmia, or by liberating into the tissues tuberculous inflammatory products which might act as specific antigens. Such a process might account for the beneficial effect of laparotomy in tuberculous peritonitis. Two observations may be quoted in favour of there being some benefit due to auto-inoculation. The first is the marked improvement in the general condition which may follow operation on tuberculous bone. This observation has been noted by others, notably Lavallo and McCrae Aitken. Certainly it has been confirmed in my experience. The effect may follow simple osteotomy through tuberculous bone without the removal of any tuberculous tissue. The second observation is the poor result which so frequently follows treatment of a tuberculous joint by amputation of the limb. Of 10 cases which had had an amputation only 3 remained permanently well. 3 died and 4 developed tuberculous lesions in other parts of the body.

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I have been much impressed by the disability that the uncorrected clubfoot produces in children in this age-group, for many of them are greatly handicapped in walking and have considerable difficulty with footwear. Moreover, they are frequently subjected to repeated manipulations, wrenchings and plaster immobilization of their deformed feet.

The results of this conservative treatment cannot be considered satisfactory. Manipulative trauma tends to produce a vicious circle of false correction, increasing fibrosis

and stiffness, followed by inevitable relapse of deformity and yet more manipulations and wrenchings.

In congenital clubfoot the deformity occurs essentially at the astragalo-calcaneo-scapoid joint. The os calcis moves with the forefoot and if the deformity at the astragalo-scapoid joint can be corrected by drawing the scaphoid around the head of the astragalus the inversion of the heel will disappear.

In the uncorrected clubfoot the scaphoid is tucked around on the inner side of the head of the astragalus and is tethered in this position by contracture of soft tissues, particularly by the inferior and internal calcaneo-scapoid ligaments. The net result of this is that the astragalus is relatively too long and it is impossible to draw the scaphoid around it.

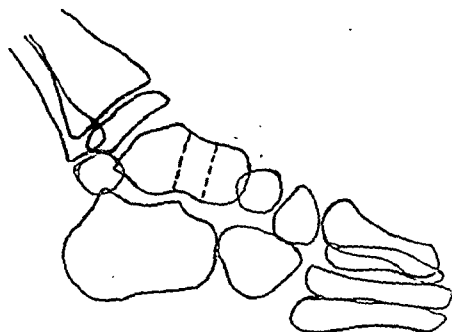


FIG. 1.

and inferior calcaneo-scapoid ligaments can be exposed and divided, thus freeing the head of the astragalus and enlarging its socket. This should allow the scaphoid to be drawn up and out around the head of the astragalus, and it will now be found that

I overcome this difficulty by shortening the astragalus by excising a section of bone from its neck (fig. 1). The operation is performed through a two-inch longitudinal incision over the neck of the astragalus, which lies, in the uncorrected clubfoot, on the outer side of the dorsum of the foot. The neck is exposed subperiosteally and bone levers, the points of which engage the sinus tarsi, are placed on either side. A section of bone, approximately one-third of an inch wide, is now removed, the proximal osteotomy being made as far back as possible in order to avoid encroaching too closely on the articular surface of the head. When the capsule on the dorsum and inner side of the astragalo-scapoid joint has been incised the internal

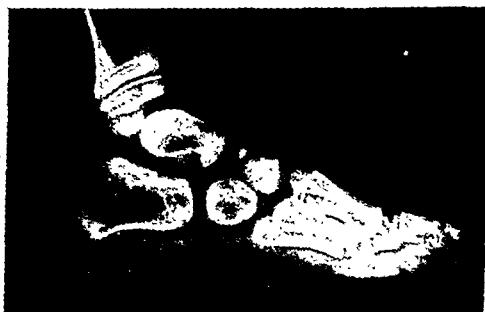


FIG. 2a.
The foot before operation. April 1940.



FIG. 2c. October 1945.

FIG. 2b. July 1940.

The foot after operation.

the gap in the neck is closed. The foot is fixed in plaster in the maximum degree of valgus, further correction of the deformity being frequently obtained at the routine change of plaster in a fortnight's time. Immobilization is maintained for four to five months and the child is then provided with an inside iron, outside T-strap and quarter-inch outside wedge on the sole of the boot.

Nine cases, in four of which the deformity was bilateral, making thirteen feet, have been treated. The operation should not be performed on children below the age of 5, the average age at operation in this series being 6. Satisfactory functional results were obtained in ten feet; in the remaining three the deformity recurred soon after operation.

It is not claimed that this treatment gives the patient anything approaching a perfect foot. It is, however, a simple method which attacks the main site of the deformity and produces a mobile, plantigrade foot on which the child can get about reasonably well until it is old enough to have a formal arthrodesis if this should be necessary. Movement at the astragalo-scapoid and sub-astragaloid joints is preserved and providing the operation is done at the right age growth is not seriously disturbed (fig. 2, a, b and c).

Sacro-iliac Arthrodesis

By P. H. NEWMAN, D.S.O., F.R.C.S.

This paper gives the results of a follow-up examination of a series of sacro-iliac arthrodesis operations performed for sacro-iliac strain by Mr. A. S. Blundell Bankart.

In every case the condition had been previously treated by one or more manipulations and had failed to respond. 36 operations were performed on 32 patients during the last ten years and during the same period approximately 500 manipulations were performed for this condition. Roughly speaking it can be said that 1 in 15 patients manipulated were eventually arthrodesed.

The Smith Petersen type of operation was used in each case and followed by a four-week rest period in bed.

RESULTS

The results were divided into cures, partial cures and failures. Cures were those who were quite definite about the relief given to them by the operation and who had suffered nothing more than a minor ache or pain in the back since. Partial cures were those who had been relieved of the original pain but complained of scar tenderness, lumbosacral aching or other non-incapacitating attacks of moderate or minor pain in this area. Failures were those not fitting into either of these two categories.

TABLE I.—SACRO-ILIAC ARTHRODESIS.
36 Operations Performed on 32 Patients.

21 were cures
6 were partial cures
6 were failures
3 were untraced
29 were females, 3 were males
Average follow-up time just over four years.

TABLE II.—SACRO-ILIAC ARTHRODESIS.
The history of an accident and the average age differed in the three groups as follows:—

History of accident	Average age
Cures 47%	31.4 years
Part. cures 0%	33.2 years
Failures 0%	42.4 years

In the tidal wave of ruptured intervertebral disc which has swept over and swamped the field of back and radiating leg pain the sacro-iliac syndrome is one of the islands which as yet remains unsubmerged. It is important therefore to have a clear concept of what is meant by sacro-iliac strain and what are the symptoms associated with it. Superficially the two syndromes may resemble each other. A history of injury followed by recurrent acute or chronic back and radiating lower limb pain. Lumbosacral pain may occur secondary to sacro-iliac conditions giving tenderness and stiffness in this area. On deeper inquiry the two syndromes differ considerably. The nature of the accident is often a torsion strain either in the standing or sitting position. It is uncommon in the male occurring almost invariably in females between the ages of 15 and 45.

and stiffness, followed by inevitable relapse of deformity and yet more manipulations and wrenchings.

In congenital clubfoot the deformity occurs essentially at the astragalo-calcaneo-scapoid joint. The os calcis moves with the forefoot and if the deformity at the astragalo-scapoid joint can be corrected by drawing the scaphoid around the head of the astragalus the inversion of the heel will disappear.

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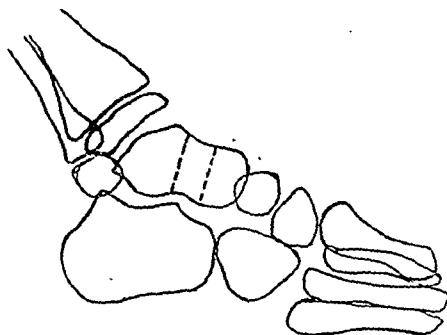


FIG. 1.

I overcome this difficulty by shortening the astragalus by excising a section of bone from its neck (fig. 1). The operation is performed through a two-inch longitudinal incision over the neck of the astragalus, which lies, in the uncorrected clubfoot, on the outer side of the dorsum of the foot. The neck is exposed subperiosteally and bone levers, the points of which engage the sinus tarsi, are placed on either side. A section of bone, approximately one-third of an inch wide, is now removed, the proximal osteotomy being made as far back as possible in order to avoid encroaching too closely on the articular surface of the head. When the capsule on the dorsum and inner side of the astragalo-scapoid joint has been incised the internal

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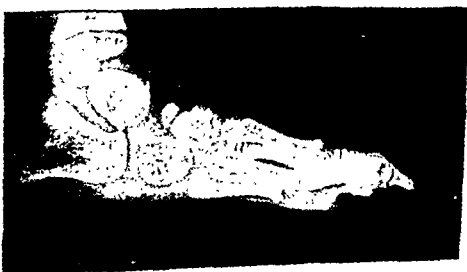


FIG. 2b. July 1940.



The foot after operation.

FIG. 2c. October 1945.

Assuming this to be the site of the true axis of rotation it is simple to imagine the relative movements of the lumbar spine and sacrum (fig. 1).

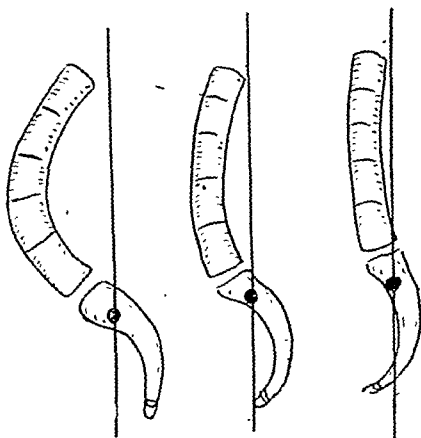


FIG. 1.—Rotation of sacro-iliac joint on transverse axis.

As the lordosis increases the greater becomes the backward tilting of the sacrum and the greater the diameter of the inferior pelvic outlet (fig. 2).

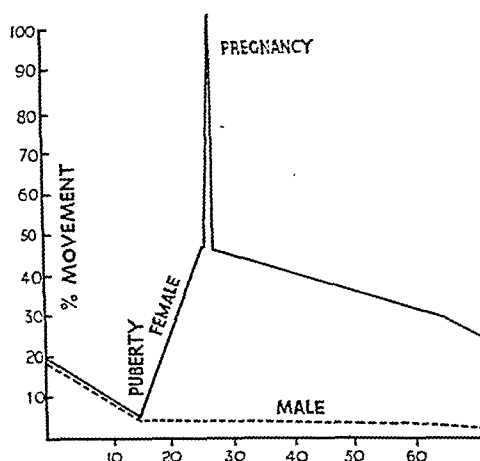


FIG. 2.—Movements of sacro-iliac joints (after Brooke, 1924).

The range of movement in relation to sex and age has been carefully plotted by Brooke (fig. 2). A small equal range is present in both sexes up to the age of puberty. In the male from then onwards there is a slowly-decreasing range until by the sixth or seventh decade it is negligible. In the female the range increases sharply up till the age of 25 and then slowly declines but even late in life there is quite an appreciable range of movement. In pregnancy the range increases tremendously to reach at term a degree twice as much as that at 25. It has been found that at full term the anterior margins of the joint can be separated by $\frac{1}{4}$ in. It is during the child-bearing age that sacro-iliac strain typically occurs. It is during the same period that there is the greatest range of movement. It is not unreasonable therefore to associate strain with the increase of the range of movement. The female needs the additional range of movement but has thereby to sacrifice stability.

The articular surfaces are irregular and present numerous crests, depressions and tubercles. When these are held tightly interlocking, as in the male, it is unlikely that

There may be a history of clicking, especially on sitting down, which is localized accurately to the sacro-iliac joint. The patient may be able to say when the joint goes in and when it goes out.

The main point in the diagnosis, however, is the site of pain and tenderness. This is invariably found just medial to the posterior superior spine or at the upper margin of the great sciatic notch. Without this it is difficult to see how the diagnosis can be made. The importance of this sign can be seen when it is realized that every patient in Smith Petersen's series of 26 cases and every patient in this series and all but one in Haldeman and Hall's series of 42 exhibited pain and tenderness over the joint.

Radiating pain.—Associated pain was found in the following areas: (1) The lumbosacral area. (2) Groin and lateral thigh. (3) Posterior thigh and leg. (4) Lateral buttock.

The lumbosacral pain can be easily explained. With a painful and guarded sacro-iliac joint the lumbosacral joint is called upon to carry out a degree of movement to which it is unaccustomed.

A pain radiating round to the groin or down the lateral side of the thigh was frequently present. Typically it was described by placing the hand round the top of the thigh pointing obliquely downwards, towards the perineum. There was no doubt about this pain for patients describing the pre-operative symptoms some long time after operation described it without being prompted by leading questions. It is peculiar that neither Smith Petersen, in his most comprehensive article on the symptomatology of this condition, nor Haldeman and Hall mention it.

It was present in 13 of the 32 patients of this series.

This pain is in the lumbar 1 and 2 distribution and the explanation of it has so far evaded me. Neither from the literature nor from various authorities has a solution been forthcoming. It cannot be described as a referred pain associated with the nerve supply of the joint as this is derived from L. 5, S. 1 and 2.

It cannot be described as a periarticular involvement of the nerves supplying this area as these have no intimate relation to the joint in question. Whatever be the origin of this pain we consider it to be a symptom typical of and valuable in the diagnosis of sacro-iliac strain.

The pain which radiates down the back of the thigh, leg and even into the foot offers three possible explanations.

- (1) A referred pain associated with the nerve supply of the joint.
- (2) A periarticular involvement of the lumbosacral, sacral 1 or sacral 2 nerve roots which have a very close relation to the joint.
- (3) An involvement of the roots by some pathological process higher up, in the nature of intervertebral arthritis or a ruptured intervertebral disc.

Sacro-iliac strain.—If an abnormal or excessively strong force is put upon a joint it is liable to produce a strain of the ligaments of that joint. This may result from an external force or by faulty mechanism due to an internal derangement. The latter case is aptly demonstrated by the loose body in the knee which insinuates itself between the moving articular surfaces thus altering the axis of rotation and throwing a tremendous strain upon the ligaments.

In the strained joint we may picture the ligaments as partially torn and pulled from their attachments. Fortunately the body has a power of recuperation and the lesion may recover completely. Should the recovery be hindered by repeated trauma, faulty posture or too long immobilization then a condition of chronic strain may result.

The movement in the sacro-iliac joint is of two types. A rotational movement and a transverse movement. The former would appear to be the more important and occurs round a transverse horizontal axis which passes through the anterior margin of the joint at the junction of the two arms of the auricular shaped articular surface at the level of the second sacral vertebra.

Brooke after examining 200 post-mortem specimens described a tubercle situated on the sacral surface which fitted into a cavity on the opposing surface at the level of the second sacral vertebra. Quain's anatomy also describes this tubercle.

Assuming this to be the site of the true axis of rotation it is simple to imagine the relative movements of the lumbar spine and sacrum (fig. 1).

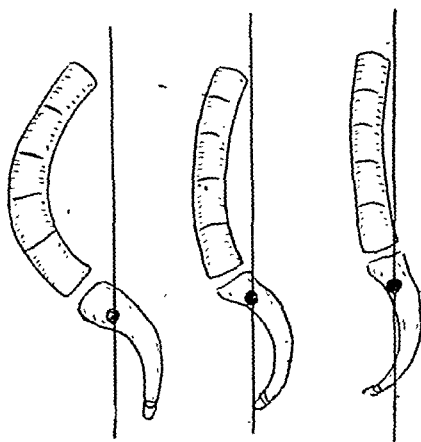


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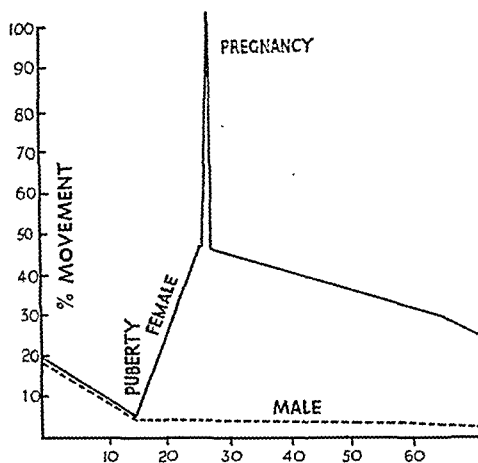


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The articular surfaces are irregular and present numerous crests, depressions and tubercles. When these are held tightly interlocking, as in the male, it is unlikely that

the surfaces will move on each other even in the severest strain. As the ligaments slacken up movement occurs and when a crest surmounts a crest then will great strain be thrown upon the ligaments of the joint.

Not only is there an increase in the vertical stretch but also sideways. When the ligaments loosen up still more crest may surmount crest with impunity and this may be imagined to be the position in a woman who feels her joint slip in and out without pain.

In conclusion I wish to stress the importance of separating the sacro-iliac from the lumbar spine syndrome.

Favourable points, indicating operation.—Age between 16 and 40. History of accident or sudden onset. Definite localized pain and tenderness. Anterior and lateral thigh pain. Clicking when sitting down. Manipulation should have failed before recommending operation.

Unfavourable points.—Age over 40. Spinal arthritis. Psychoneurotic type. A long history of poorly localized or generalized pain. A demoralizing gynecological or obstetrical history.

In carefully selected cases sacro-iliac arthrodesis is a good operation.

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Arterial Advances of Orthopædic Concern

By SOL. M. COHEN, M.A., F.R.C.S.

CLINICAL CONSIDERATIONS

FROM Lewis' vast contributions on the principles of the circulation I will mention only a few fundamental points:—

(a) The skin and muscle circulations are each under triple control—local chemical, hormonal and nervous. Changes may occur in the skin with opposite or no changes in the muscle, and a warm-skinned limb may have poor or even dead muscles beneath. A relatively small blood-flow is sometimes sufficient to maintain a normal skin temperature. The local metabolites of muscle exercise, in the main, regulate the muscle circulation. The orthopædic surgeon has in recent years applied this knowledge, particularly in reabbling. Quite ten years ago Fagge, of Guy's, said that: "Physiological rest does not imply immobility . . . it is the acquisition of a state of *eased function* favourable to repair."

(b) After arterial arrest in the ischæmic limb loss of sensation followed by motor power does not ensue until fifteen to thirty minutes later, due to interference with nerve conduction; and loss of power is often a valuable signal as to whether the plaster or the splint is too tight.

(c) The ischæmic limb may feel to the patient nerveless and dead; there will be pain, only if the limb has been exercised to arterial arrest.

(d) Tissues with specialized function vary in the time that they can withstand arterial arrest. Muscle will survive six to ten hours, nerve twelve to twenty-four hours, skin twenty-four to forty-eight hours.

(e) The dangers of overheating ischæmic tissues are appreciated to-day, but the pendulum has swung extravagantly to extreme cold. Icing is dangerous; tissues are damaged directly, metabolite formation interfered with, and oxyhamoglobin will not dissociate below 10° C. Icing, I believe, should be reserved for the dead limb; amputation under ice anæsthesia is a first-class new method in selected cases. So much for the clinical facts.

General condition and limb survival.—We now realize the importance of the general condition for the survival of the limb. Rapid massive blood transfusions are an enormous advance. Powerful peripheral vasoconstriction otherwise clinically is maintained

in the large vessels and the arterioles. Shakespeare seemed to know something of this when he made Hamlet say:

"My fate cries out,
And makes each petty artery in this body
As hardy as the Nemean lion's nerve."

Experiment seems to indicate that one of the most important factors in collateral vessel dilatation is a good pressure head within the vessel lumen. With a sluggish circulation the arterial inflow must, to a great extent, be dependent on the venous outflow. It does not seem good advice, therefore, to nurse the limb, as was advocated both in the B.L.A. and Middle East campaigns, in the dependent position. Such venous stagnation, in an area filled with all the factors favouring thrombosis, is likely to prejudice the already sluggish arterial inflow. We must not forget, too, the value of the lymphatic system as an accessory circulation—a scavenger; elevation of the limb (heart-level) will assist the flow and compensate to some extent the ischæmic loss of muscle power. Orthopædists are aware of the stiff clawed toes in many of these cases, due to the periarticular coagulation of the stagnating lymph; such joints need to be passively moved in the ischæmic limb, just as do the joints after nerve section.

The role of the sympathetic system.—Modern opinion views the sympathetic system more and more as an effector mechanism, with no sensory fibres. Sympathetic block or section increases the skin circulation, is of value for the skin or the hand-foot lesion, but has little effect on the muscle lesion. Boyd [1] has recently urged that no major vessel should be tied without at the same time sympathetic interruption. I do not agree. To dilate the skin vessels—which of course we can achieve as easily, reflexly, by merely heating the patient—may be hazardous. It leads to pooling of blood and its soaking up in a spongy unessential area, thus depriving the deeper vessels. With any vessel ligature, arteriography shows that the blood seeks to find its way into the main deeper channels; unless that flow is maintained, fairly briskly, thrombosis ensues. I need only quote the latest paper of 100 major vessel injuries in war by Rose, Hess and Welch [2]. Their limb mortality, despite routine sympathetic blocks, is high, and I quote their blunt comment "in no case did this procedure appear to reverse the progress from an avascular state in patients with severed arteries."

DeBakey and Simeone [3] have analysed 2,471 arterial injuries in American battle casualties; 30 out of 42, who had sympathectomies, lost their limbs (the severer cases may, of course, have been selected for this procedure). The real test of the value of sympathetic block is as to whether it could save the limb with popliteal vessel injury. I can quote a large number of cases where this procedure made no difference; associated damage to the collaterals had long sealed the fate of the limb. Sympathectomy preliminary to operation for the arterial or arteriovenous aneurysm was much mooted in the early years of the war; it seems unnecessary. Elkin [4], who has probably had the most extensive experience any surgeon is ever likely to have, has published astonishing figures. He has treated some 106 false aneurysms in which some form of major vessel interruption became necessary. In no case did he perform sympathectomy, none developed gangrene or other untoward ill-effects in the distal limb. Neither Learmonth [5] nor Maybury [6] now do pre-operative sympathectomies. I would touch also on one further fact about sympathectomy. Pre-ganglionic section is now the fashion. Everyone who has done any sympathectomies will have observed, and anatomists (Pick and Sheehan [7]) have recently confirmed, the extraordinary variations in the anatomy of the ganglia and the rami. We run considerable risk of doing an incomplete operation, and ganglionectomy may well come into favour again. The results after pre-ganglionic section have not been startlingly better; even with this procedure there is an increased sensitivity to adrenaline-like substances. Grimson [8], in a recent very able review, backs with emphasis the radical ganglionectomy procedure. Certainly for the leg I invariably remove, as well, the fourth lumbar ganglion. Lastly, it is perhaps right that we maintain an attitude of scepticism to the idea that sympathetic fibres have remarkable navigational qualities through fibrous tissue, and can seek and find out the opposite cut end. Its powers of regeneration are no greater than that of any peripheral nerve. This "apparent" regeneration is capable of simple explanation. Any operation on the sympathetic system, involving as it does much stripping and bruising of the sympathetic trunk, must necessarily contuse or render ischæmic the ganglia and fibres. Nerve conduction is interfered with, and the "incomplete" operation gives at first a good result: later, the nerve fibres within intact sheaths recover and spoil the end-result.

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Advances in surgery of access.—This has been developed particularly for dealing with the arterial aneurysm or the arteriovenous fistula.

(a) Proximal control is now invariably sought before exposing the aneurysm sac. For the common femoral aneurysm I would endorse the advice of Holman [14], that both the common iliac and external iliac need temporary ligatures. I would commend this to the orthopaedic surgeon for use prior to hip disarticulation, and it may well be of assistance for reconstructive operations on the hip-joint. The vessels are easily exposed by a transverse gridiron incision and extraperitoneal stripping. A word of warning. Tape over a segment of rubber tubing is these days preferred to the Crile clamp. The tape knot, however, slides in jerky fashion, and I have myself tied it too tightly and damaged the vessel. I now paraffin the tape, and Crile's clamps do not damage the vessels.

(b) Division of the clavicle or excision of a middle segment is a measure giving a first-class exposure for the axillary or subclavian aneurysm. Segment excision seems preferable, and I have been astonished at the painless free movements without loss of power after operation. This operation has been well described by Elkin [4a] recently.

(c) Excision of the upper end of the fibula too is a very useful measure for exposure of the aneurysm of the anterior tibial artery near its origin (Elkin [4b]).

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In vascular operations for the thigh the ordinary blood-pressure tourniquet band is too short, and two blood-pressure bags—front and back—are useful. Where there is too much bleeding, and one is anxious to get the vessel point, I advise the use of two suckers; diathermy is invaluable; drainage is a courier of sepsis; prophylactic penicillin after the vascular operation is to be recommended. To the surgeon's armamentarium has also been added in this war fibrin foam as a hæmostatic agent; we now have an absorbable pack—oxidized cellulose—and recently gelatine sponge [16] has given us for the thrombin a matrix which is universal, free from danger of antigenicity, with little local tissue reaction, and readily procurable. When it comes to amputating the ischæmic limb, experience gathered in the B.L.A. campaign seems to be of value; by dissecting skin flaps, coring out the dead muscle, a skin-bone stump can often be left, which although short is still very useful.

Muscle biopsy has been actively undertaken in World War II, and has taught us not only about recovering nerve lesions, but also about the distinctive appearance of dying ischæmic muscle. Whether temporary arterial or venous obstruction be responsible for the Volkmann's lesion they both may give the same ultimate result, although there is some difference in the primary microscopical picture [17]. These cases should not be stretched too early. No amount of splinting will check the impending Volkmann's contracture in the leg, and much harm may be done to the anæsthetic sole by excessive splintage. Untoward effects in the limb may follow the ischæmia, even if no gangrene or Volkmann's contracture result, and Athol Parkes [18] has drawn attention to the anæsthesia, the delayed pain responses and intrinsic muscle atrophy that may follow the too tight plaster or the very œdematous limb. I have seen the same effect even when there has been no plaster or excess œdema, and these nerve effects may be directly consequent on the ischæmia itself.

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Vascular reflexes.—Before the last war there was much ado about local reflexes arising from the bruised vessel and reflex spasm of the collaterals; arterectomy to break such reflex arcs was usual. It seems a bad operation; if there is any collateral vessel damage the surgeon has added the *coup de grâce* to the limb (Cohen [9]).

Lewis declared that there was no physiological sanction for this theory of reflex spasm of the collaterals from the bruised vessel. An advance in the treatment of the arterial bruise is the advice of Maybury [6] to oversew it with muscle or local tissue, to assist the localization of the hæmatoma and the formation of an aneurysm, in the event of rupture. Such a bruised vessel does not necessarily predispose to secondary distal clot formation, and I have seen several cases where only a local blockage was subsequently maintained.

Arterial spasm.—There are two types of arterial spasm: (a) benign or segmentary spasm; there is a direct vessel blow with twanging by bone fragment or "near miss". If found at operation—as for the supracondylar fracture—experience seems to indicate that it is best left alone. Such exploration is of value, for time and again the vessel is found trapped between the bone ends or sharply angulated (the latter stretching will obliterate also the collateral vessel mouths—much as stretching rubber tubing narrows it—and explains why in some cases arterectomy appears to have been of value). (b) The second type of spasm is reflex; the local tissues have here received a severe local blow, but the cushioned vessel has had no direct damage. Such arterial spasm is often malignant in its obstinacy.

Arteriography.—Diodone—an organic iodine compound—is a safe medium—I use "Pyclosil" 35%. Arteriography is of use for:

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Heparin.—Unfortunately this has been in short supply during the war. Interrupted injections are unreliable, and the continuous drip is to be preferred. The recent introduction of Pitkin's menstruum as a conveyer for heparin [10] allows it to be deposited subcutaneously and to maintain a uniform therapy. As, time and again, thrombosis in the artery or veins seals the fate of the limb, heparin may well come to play an important role, not only after suture, but also for the limb with sluggish circulation. As orthopaedic surgeons come to evaluate their results in their older patients they will find that pulmonary embolus takes quite a toll. In the intratrochanteric type of fracture the Americans already point to its high incidence, and list it as the most frequent cause of death (Golodner, Morse and Angrist [11]). Heparin may be used but thrombosis often comes on, even so, some time after its discontinuation. Interruption of the femoral vein is a new safety measure that I have myself used, and feel that it has great possibilities.

Vein grafting.—The vitallium cannula method of vein grafting has been hailed by Matas—the Nestor of Vascular surgery—as "the greatest advance in peripheral vascular surgery in the last twenty-five years". Blakemore and Lord's [12] results experimentally, and in the cases published, are amazing and its use by Whipple in portal hypertension has opened up a complete new approach to the subject. From the experience of American and Canadian friends one can say that: (a) The technique is not easy, and unless carried out carefully may lead to destroying or blockage of important collaterals. (b) Where the ligature holds the cannula the vessel sloughs and the graft lies somewhat perilously after the fourth day. Rose, Hess and Welch [2] have reported on its use in 8 war injuries; 1 died on the table, and 5 out of the other 7 developed gangrene. They consider that thrombosis and spasm caused the death of these limbs. DeBakey and Simeone [3] have collected information on 40 cases—the limb mortality was 57.5%. However, there is no doubt that vessel ligature in war carried an extraordinarily high limb mortality; 50 to 70% for the femoral, and higher for the popliteal. Arterial sutures should receive more trial in civil surgery. When this is not possible, the experience of Mustard [13] (3 cases), American surgeons (14 cases)—and I have had one case—of using glass, or possibly plastic cannula, may revive a useful method for tiding the limb over. The dislocated knee with popliteal artery injury, in my experience, usually has extensive damage to the collaterals; if such limbs are to be saved, then some form of vessel bridge seems essential.

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(c) In arteriosclerotics in deciding as to whether a below-knee amputation will be safe. Time and again in the arteriosclerotic, one finds a local block in the region of Hunter's canal. In some of these cases it would appear that vein grafting may become a practical possibility. (Dickson Wright has already done this.—Personal communication.)

Heparin.—Unfortunately this has been in short supply during the war. Interrupted injections are unreliable, and the continuous drip is to be preferred. The recent introduction of Pitkin's menstruum as a conveyer for heparin [10] allows it to be deposited subcutaneously and to maintain a uniform therapy. As, time and again, thrombosis in the artery or veins seals the fate of the limb, heparin may well come to play an important role, not only after suture, but also for the limb with sluggish circulation. As orthopaedic surgeons come to evaluate their results in their older patients they will find that pulmonary embolus takes quite a toll. In the intrathrochanteric type of fracture the Americans already point to its high incidence, and list it as the most frequent cause of death (Golodner, Morse and Angrist [11]). Heparin may be used but thrombosis often comes on, even so, some time after its discontinuation. Interruption of the femoral vein is a new safety measure that I have myself used, and feel that it has great possibilities.

Vein grafting.—The vitallium cannulae method of vein grafting has been hailed by Matas—the Nestor of Vascular surgery—as "the greatest advance in peripheral vascular surgery in the last twenty-five years". Blakemore and Lord's [12] results experimentally, and in the cases published, are amazing and its use by Whipple in portal hypertension has opened up a complete new approach to the subject. From the experience of American and Canadian friends one can say that: (a) The technique is not easy, and unless carried out carefully may lead to destroying or blockage of important collaterals. (b) Where the ligature holds the cannula the vessel sloughs and the graft lies somewhat perilously after the fourth day. Rose, Hess and Welch [2] have reported on its use in 8 war injuries; 1 died on the table, and 5 out of the other 7 developed gangrene. They consider that thrombosis and spasm caused the death of these limbs. DeBakey and Simeone [3] have collected information on 40 cases—the limb mortality was 57.5%. However, there is no doubt that vessel ligature in war carried an extraordinarily high limb mortality; 50 to 70% for the femoral, and higher for the popliteal. Arterial sutures should receive more trial in civil surgery. When this is not possible, the experience of Mustard [13] (3 cases), American surgeons (14 cases)—and I have had one case—of using glass, or possibly plastic cannulae, may revive a useful method for tiding the limb over. The dislocated knee with popliteal artery injury, in my experience, usually has extensive damage to the collaterals; if such limbs are to be saved, then some form of vessel bridge seems essential.

JOINT DISCUSSION No. 4

Section of Neurology with Section of Orthopædics

Chairman—J. PURDON MARTIN, M.D., F.R.C.P.

(President of the Section of Neurology)

[March 7, 1946]

DISCUSSION ON SPINAL CARIES WITH PARAPLEGIA

Professor H. J. Seddon, Nuffield Department of Orthopædic Surgery, Oxford: *The pathology of Pott's paraplegia.*

Between 1870 and 1900 the pathology of Pott's paraplegia attracted great attention: cellular pathology was making rapid strides, the disease was common and opportunities for post-mortem examinations not infrequent. The questions at issue were whether the lesion was a true myelitis, or the result of a pachymeningitis, or due to compressive changes affecting the arteries, veins or lymphatics of the spinal cord.

During the present century interest has flagged; however, the nature of cord compression in general has been worked out thoroughly, notably by Purves-Stewart and Riddoch (1923); in 1925 a valuable monograph on Pott's paraplegia was published by Butler and I published papers, covering most aspects of the disease, which were based on a review of 186 cases. Since that time I have seen some 40 more cases but what has been learned from them has concerned treatment rather than pathology, and the same seems to be true of other recent observers.

The thing that has emerged most clearly is the fairly sharp distinction between paraplegia occurring during the active phase of the spinal disease and that appearing at a much later date when, to all appearances, the vertebral lesion is well healed.

PARAPLEGIA OF EARLY ONSET

The intraspinal abscess.—Everyone is familiar with paraplegia occurring during the active phase of the spinal disease; indeed, derangement of locomotion is sometimes the presenting symptom. And it will not be disputed that in most cases the cause of the paraplegia is a tuberculous abscess, provided that the term abscess is used in a fairly wide sense so as to include any tuberculous inflammatory mass whether its contents are fluid or semi-solid. The abscess is usually in the thoracic region, where three factors favour involvement of the spinal cord: (1) The narrowness of the spinal canal; (2) the anterior concavity of the vertebral column which encourages angulation at the site of disease (fig. 1) and the squeezing of inflammatory products towards the cord (here it may be mentioned that there is clinical evidence (Goldthwait, 1889) to show that this factor is significant); and (3) the close confinement of the abscess by the stout anterior common ligament; where an abscess can escape—into the psoas muscle, for example—paraplegia does not occur and I have yet to see an exception to the rule that paraplegia due to compression by an abscess cannot coexist with a clinically palpable abscess.

Very rarely, the primary focus is beneath the posterior common ligament (fig. 2), and a few cases have been recorded (Fischer, 1919; Vincent and Darquier, 1925; Seddon, 1935) in which radiographs revealed no bony lesion until long after the onset of the paraplegia. Clinically, there is no direct way of distinguishing this type of Pott's paraplegia (what we have called the *spinal tumour syndrome*) from that due to an intraspinal neoplasm and the diagnosis can be made only by laminectomy. Almost equally rare are those cases in which the disease begins in a *neural arch* (Seddon, 1935), the abscess

[June 15, 1946]

MEETING AT WINGFIELD MORRIS ORTHOPÆDIC HOSPITAL, OXFORD

The following *short papers*, illustrated by many cases, were read as follows:

Slipped Upper Femoral Epiphysis.—Mr. W. B. FOLEY.

Treatment of Acute Osteomyelitis with Penicillin.—Mrs. AGERHOLM (for Professor J. TRUETA).

Peripheral Nerve Grafting Operation.—Professor H. J. SEDDON.

Muscle Transplantation: Portion of the Pectoralis Major Muscle to Paralysed Biceps (With Film).—Professor H. J. SEDDON.

Organization of a Regional Accident Service.—Group Captain J. C. SCOTT.

Demonstration of a Self-Propelling Surgical Chair in its Early Stage of Construction.—Mr. GIRDLESTONE.

Tendon Transplantation for Radial Paralysis.—R. B. ZACHARY, F.R.C.S.

The classical method of tendon transplantation in radial paralysis is to transfer the pronator teres tendon into the extensors of the wrist, and to use flexor carpi ulnaris and flexor carpi radialis tendons for extension of the fingers and thumb. There is no argument about the value of using the pronator teres tendon for extension of the wrist, but the transplants to the fingers and thumb are not always satisfactory. We have found that if the palmaris longus is absent the transplantation of the tendons of both wrist flexor muscles leaves nothing to control the wrist, so that when an attempt is made to extend the fingers, the wrist goes into acute dorsiflexion and the fingers remain flexed at an angle of about 40 to 60 degrees. Moreover, this action of the wrist is the reverse of the normal process, for in the normal individual there is a tendency for the wrist to come to the neutral or slightly flexed position on opening the fist. It is clear that the fault is not a technical one such as slipping of the tendons, for if the wrist is passively held in the neutral position full extension of the fingers can be achieved.

When the palmaris longus muscle is present, the results are better but still uncertain. Some patients can control the wrist fairly well with the palmaris longus but others cannot, so that in this group of cases there are still a number in which the wrist-joint tends to dorsiflex when extending the fingers, with the result that the extension of the fingers is not complete.

In those cases where the flexor carpi radialis tendon has not been used, its control of the wrist allows full extension of the fingers and, moreover, strong active flexion of the wrist is maintained. It is, therefore, our policy in tendon transplantation for cases of radial paralysis to retain the flexor carpi radialis in its normal place and to use the palmaris longus as a transplant for the thumb if it is present. If the palmaris longus is absent, we have used the flexor carpi ulnaris for the thumb as well as for the fingers with success.

[June 19, 1946]

MEETING AT ROYAL SOCIETY OF MEDICINE, 1, WIMPOLE STREET, W

Dr. Sterling Bunnell (San Francisco) gave an Address entitled *Certain Aspects Of Hand Surgery In World War II*. This was summarized in the *Lancet*, 1946 (ii), 53.

found a case in which almost the whole mass of an *intervertebral disc* had been pushed backwards and was the cause of the compression. Lastly, a vertebra riddled with tuberculous disease may suddenly *collapse like a concertina* (fig. 7), causing a paraplegia of rapid onset (Girdlestone, 1931; Butler, 1935).



FIG. 5.

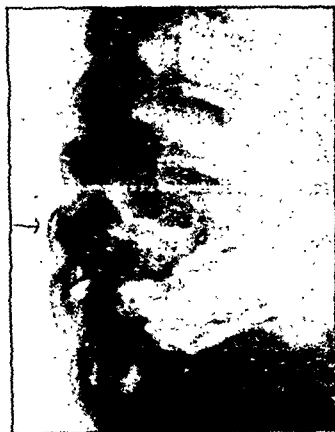


FIG. 6.



FIG. 7.

FIG. 5.—Pathological dislocation of the thoracic spine causing compression of the cord. In this case the posterior common ligament was intact and the cord lesion was, therefore, purely mechanical in origin.

FIG. 6.—Radiograph of spine showing pathological dislocation. The nature of the lesion was confirmed at operation; it was also found that an abscess had penetrated the posterior common ligament—in contrast with the case shown in fig. 5, though it was doubtful whether this factor contributed to compression of the cord.

FIG. 7.—Concertina collapse of the eighth thoracic vertebral body. Diagnosis of tuberculous disease confirmed histologically. (Reproduced by permission of Mr. R. W. Butler.)

PARAPLEGIA OF LATE ONSET

In these cases the patient usually has a considerable deformity (fig. 8), he has been getting about well for a number of years after being treated for spinal caries, and then



FIG. 8.

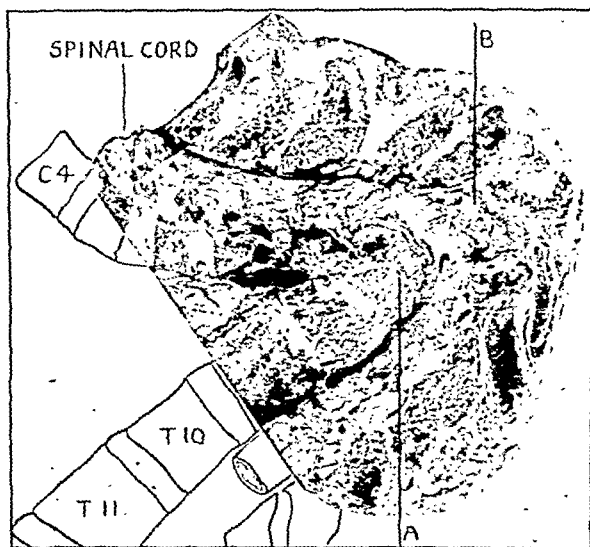


FIG. 9.

FIG. 8.—The sort of case of old tuberculous disease of the spine in which paraplegia of late onset is not uncommon. When this photograph was taken the patient was beginning to complain of weakness of the lower limbs. A typical paraplegia developed subsequently.

FIG. 9.—The characteristic lesion in paraplegia of late onset. Although there is a bony spur in the floor of the spinal canal (a), the cause of the compression is an abscess (b), lying beneath the laminae.

compressing the cord from behind; and although radiographic changes (fig. 3) are present they have sometimes been overlooked.

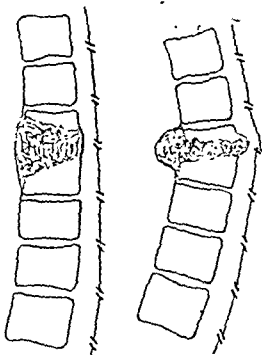


FIG. 1.



FIG. 2.



FIG. 3.

FIG. 1.—Diagram showing how angulation of the spine may squeeze tuberculous material into the spinal canal.
 FIG. 2.—Spinal tumour syndrome. The patient was a woman aged 23 years who died as a direct result of the paraplegia. Although there is widespread infection of the bodies of the 4th and 5th cervical vertebrae, as shown by the loss of normal trabeculation and some erosion of the posterior surfaces of both bodies, nothing abnormal could be detected radiographically. The abscess responsible for the compression of the cord is well shown (Guy's Hospital Museum).
 FIG. 3.—Radiograph of the spine of a boy aged 9 years who was admitted to hospital with incomplete paraplegia. Destructive lesion of pedicles and arch of Th. 8; a typical lesion of the vertebral bodies appeared later. (Dr. J. G. Johnstone's case, Princess Mary's Hospital, London County Council, Margate.)

Mechanical accidents.—Although a tuberculous abscess is the commonest cause of paraplegia of early onset there is a group of cases, sufficiently large to merit serious attention, in which some kind of mechanical accident has occurred as a result of the solution of continuity of the spine. The most dramatic were those cases, now very rare, in which the disease began in the atlas or axis, paralysis of all four limbs or even death occurring without any warning as a result of pathological luxation between the suboccipital vertebrae. Until the publication of our papers it was not recognized that similar though less dramatic *pathological dislocation* sometimes occurs at the usual site of disease (figs. 4, 5, and 6) producing a compression of the cord in which the tuberculous

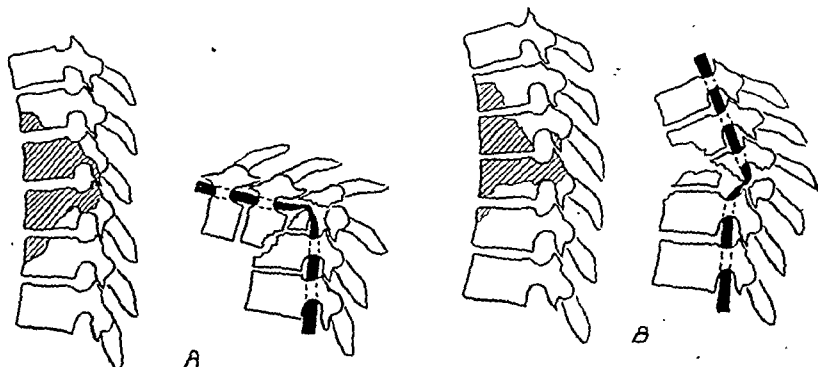


FIG. 4.—Diagram showing the two ways in which compression of the cord may result from pathological dislocation in tuberculous disease of the thoracic spine. The shaded areas represent bone destruction: (a) the upper segment of the spine has slipped downwards and forwards (compare fig. 5); (b) the upper segment has slipped downwards and backwards (compare fig. 6). (Diagram reproduced by permission of Mr. R. W. Butler.)

disease as such may play no part whatever. We have records of a number of cases in which this state of affairs resulted from incautious laminectomy, the surgeon who removed all that was holding the vertebral column together having neglected adequate post-operative fixation. Similarly the retropulsion of a *sequestrum* may compress the cord (Sorrel and Sorrel-Déjérine, 1932; Calvé—see Butler, 1935), and five years ago I even

found a case in which almost the whole mass of an *intervertebral disc* had been pushed backwards and was the cause of the compression. Lastly, a vertebra riddled with tuberculous disease may suddenly *collapse like a concertina* (fig. 7), causing a paraplegia of rapid onset (Girdlestone, 1931; Butler, 1935).



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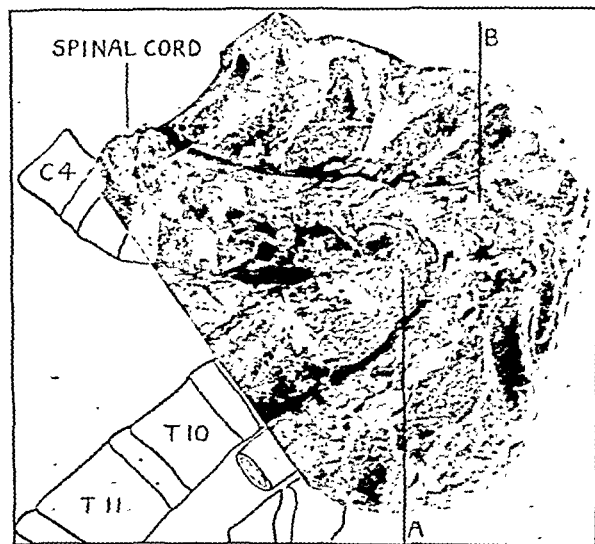


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FIG. 9.—The characteristic lesion in paraplegia of late onset. Although there is a bony spur in the floor of the spinal canal (a), the cause of the compression is an abscess (b), lying beneath the laminae.

complains of some difficulty in walking. At first I thought that this late paraplegia was somewhat akin to traumatic ulnar neuritis; in this I was supported by the findings in a case (Seddon, 1935) in which there was undoubtedly stretching of the cord over a bony prominence in the floor of the spinal canal, and this case was cured by removal of the spur. Sorrel-Déjerine reports a similar case but there is now no longer any doubt in my mind that Butler is right in attributing most of these late paraplegias to reactivation of a small tuberculous mass inside the spinal canal. The environment of the cord is not a happy one, its circulation must be precarious, and very little compression will be required to interrupt its conductivity. A typical example is shown in fig. 9.

Two points in favour of Butler's hypothesis and against mine are that a paraplegia of late onset not infrequently clears up with rest in the same way as an early paraplegia due to compression by an abscess. And in some intractable cases on which I have operated I found the tuberculous focus which he described, and recovery followed its removal although no attempt was made to remove the bony ridge in the floor of the spinal canal.

The question of pachymeningitis is deliberately left to the last. Anyone familiar with the morbid anatomy of paraplegia of early onset must have been impressed by the remarkable appearance of the dura mater in many of the cases. Its thickness is greatly increased and the outer surface presents the typical shaggy appearance of tuberculous granulation tissue. But it has long been known that the tuberculous material may be dissected off the dura with remarkable ease (fig. 10), leaving behind a clean fibrous



FIG. 10.—Paraplegia of early onset due to compression by an abscess. The tuberculous process, shown below, has not invaded the dura, shown above, and there is even a line of cleavage visible between the two strata of tissue. (Reproduced by permission of Mr. R. W. Butler.)

membrane which seems to possess the most astonishing powers of resistance to tuberculous infection. Clearly then this is not pachymeningitis; nothing less than an interstitial tuberculous infection of the dura merits the term. With one notable exception

all recent observers are sceptical about tuberculous pachymeningitis; but the exception must be examined with care since Sorrel-Déjerine bases her classification of Pott's paraplegia on the assumption that pachymeningitis is constantly found in those cases in which the onset is late and insidious. This assumption rests on the observation of two undoubted cases of pachymeningitis. In one the cord was compressed by a bony spur opposite which was a patch of pachymeningitis; in the other, there was an anterior subluxation of the fifth cervical vertebra with consequent deformation of the cord, and an old abscess firmly adherent to the dura, the outer layers of which were infiltrated by the disease, the inner layers and internal surface being entirely normal. Although no one examining the evidence can deny that these are cases of genuine tuberculous pachymeningitis, it must be clear that in the presence of the other conditions mentioned there are hardly sufficient grounds for saying that the pachymeningitis was the cause of the paraplegia. That both these patients developed paraplegia late in the course of the disease and showed among other things patches of pachymeningitis is no proof whatever that the cord lesion was due to the tuberculous involvement of the dura mater. The condition is one that neither Butler nor I have seen.

It has been supposed that the dense fibrosis and annular constrictions of the dura sometimes found associated with paraplegia of late onset represent the healed stage of pachymeningitis. Yet there is no reason why these conditions should not result from the healing of an abscess that has been in contact with or even encircling the cord. Macewen (1888) and others who have performed laminectomy in such cases were able to strip off the fibrous tissue without opening the dura and so relieve the compression, further evidence in support of the generally accepted view that the tuberculous process is essentially epidural. The conclusion is that pachymeningitis is a very rare condition and its causal relations to paraplegia have not yet been established.

CHANGES IN THE SPINAL CORD

It must be conceded that paraplegia of early onset can occur in the absence of compression. This was demonstrated by Butler in two cases that came to post-mortem, and in a recent case of mine quite severe paraplegia was present—which recovered spontaneously—although lumbar puncture showed no evidence of spinal block. These findings have revived interest in the theory that paraplegia may be due to oedema of the cord, though we cannot tell whether the oedema is merely the result of the hyperæmia that is found in all tissues adjacent to a tuberculous focus or to a local toxic process. In Butler's cases, to which he has allowed me to refer, there was a curious vacuolation of the white matter of the cord (fig. 11) and a higher magnification (fig. 12) suggests

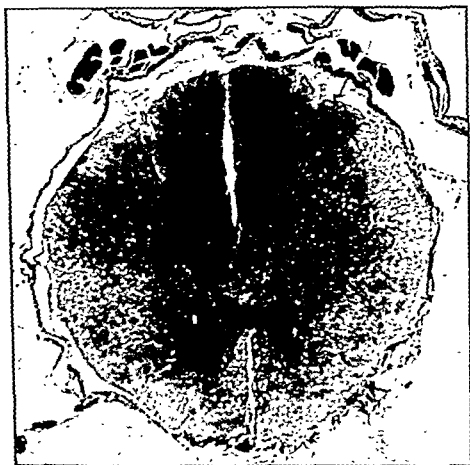


FIG. 11.

FIG. 11.—Paraplegia of early onset without compression of the cord. Section at the level of the disease from a woman aged 38, with an early mid-thoracic lesion admitted to the National Hospital, London, with paraplegia of six months' duration. Tuberculous granulation tissue was present in the extradural space, but there was no mechanical compression of the cord. The appearance of vacuolation in the anterior and lateral tracts of the cord is well shown. (For this and the following illustration the writer is indebted to Dr. J. G. Greenfield and Mr. R. W. Butler.)

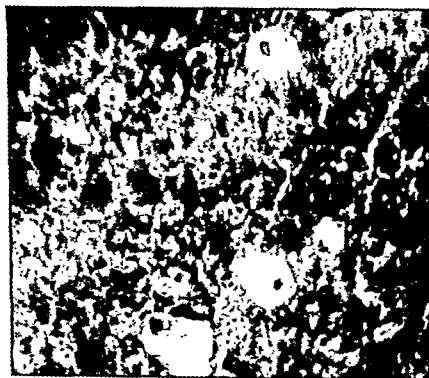


FIG. 12.

FIG. 12.—Higher magnification of cord shown in fig. 11. The clear circular spaces give the appearance of vacuolation and it seems that the myelin sheaths are chiefly involved, the axis cylinders persisting even where the swelling is greatest.

that it is due to some change in the myelin, which swells considerably, leaving the axon still visible but not intact, since the process leads to the ordinary ascending and descending degeneration. Nevertheless, however the derangement of the cord may start, when an abscess is the causal agent, a true mechanical compression usually develops sooner or later, in no way different from that resulting from other kinds of extradural swelling. Where there has been what I have called a mechanical accident the damage to the cord is, of course, purely mechanical too.

In one case there was no doubt that a profound and rapidly fatal tetraplegia of very rapid onset was due to thrombosis of the vessels of the cord. A youth aged 18 years developed caries of the fourth to sixth cervical vertebrae, with a large abscess in the neck. This abscess was in contact with the vertebral artery (fig. 13) which was found to be thrombosed, as were a spinal branch and the medullary vessels at the same level. There



FIG. 13.—Infective thrombosis of the vertebral artery spreading along the spinal branch and involving most of the small vessels of the corresponding segment of the cord. Transverse section through the vertebral artery and an intervertebral foramen.

was no mechanical compression of the cord. This type of lesion may be more common than we suspect.

In considering the change in paraplegia of late onset Butler has drawn attention to the remarkable longitudinal shrinkage of the cord. Seeing that in most of these cases a number of vertebral bodies have been destroyed it might be supposed that the cord would be relatively too long for the spinal canal and that even the nerve roots would not bind it firmly to the anterior wall. Yet we find that the cord is always closely applied to the bony spur which is why I thought at first that we were dealing with a true bony compression. I am bound to agree with Butler that there is a widespread change in the cord which, for want of a better term, he has called atrophy, though we know nothing of its precise nature.

From the therapeutic standpoint the problem is to know what degree and duration of compression the cord can tolerate before serious permanent changes occur. We know that many cases of paraplegia recover spontaneously because the abscess shrinks as the tuberculous process becomes quiescent; furthermore there are weighty reasons why extensive operative decompression is less desirable than in other forms of cord compression. Yet an expectant policy can be carried too far. Charcot (1880) examined the cord from a case in which the patient had recovered from a paraplegia two years before he died from hip disease, and at the level of the lesion found that it was reduced to about one-third of its normal diameter, that there was extensive gliosis and obvious ascending and descending degeneration. Kröger (1888) describes another less striking case in which the only abnormality at the level of the lesion was thickening of the walls of blood-

vessels. A third case (fig. 14) I saw myself. She was treated conservatively, and after her death from amyloid disease Dr. Greenfield examined the cord. The changes seen were much the same as those described by Charcot and—it will be noted with interest—there was considerable epidural fibrosis. We cannot be satisfied with results of this kind. The truth of the matter was that the patient still had a mild paraplegia—recovery was only relative—and the condition of her cord was so precarious that a recrudescence



FIG. 14a.

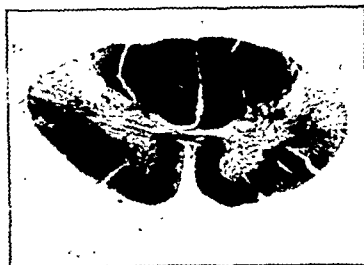


FIG. 14b.



FIG. 14c.

FIG. 14.—The cord from a patient regarded as having recovered from paraplegia of early onset, the treatment having been conservative throughout. (a) Transverse section of the cervical cord showing widespread ascending degeneration especially in the columns of Goll. (b) Transverse section through the upper lumbar cord showing extensive descending degeneration in the lateral columns. (c) All that was left of the cord at the level of the lesion Th. 4-6. The cord was reduced to one-quarter of its normal cross-section area, all trace of the normal arrangement of white and grey matter has disappeared, and the number of myelinated fibres, stained black, traversing the zone is very small. The amorphous material surrounding the cord is mostly fibrous tissue.

Acknowledgments.—Figs. 4, 6, 7, 10, 11, 12 and 13 have appeared in *Brit. J. Surg.*, 1934-5, 22, and are reproduced by permission of Messrs. Wright & Sons.

of compression might have finished it off completely. This, I think was an example of conservatism carried too far.

In paraplegia of early onset the relation of the pathological state with the diagnosis and appropriate treatment may be summarized as follows:

Abscess.—			Diagnosis	Treatment
Usual type	no difficulty	conservative: if severe, decompression laminectomy laminectomy
posterior spinal disease		
spinal tumour		
Mechanical accidents.—				
subluxation	difficult	decompression essential
sequesterum		
prolapsed disc	impossible	
concertina collapse	rapid onset of paralysis characteristic radiographic appearance	
				rapid onset of paralysis with only the usual radiographic changes
Thrombosis				decompression may be of value
				useless

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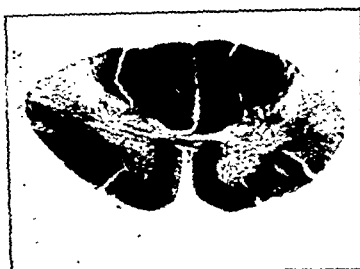


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prolapsed disc	...				
concertina collapse	...	rapid onset of paralysis characteristic radiographic appearance	rapid onset of paralysis with only the usual radiographic changes	decompression may be of value	
	...				
Thrombosis	...			useless	

From the therapeutic standpoint the figures from Butler's and my series give a rough idea of the relative sizes of the three main groups of cases. The incidence of paraplegia in the 186 cases was 193, several patients suffering more than one attack of paralysis. There were 76 cases of paraplegia (39%) of early onset in which spontaneous recovery occurred, the causal factor in most of them being almost certainly an abscess. There were 21 cases (11%) in which a paraplegia of early onset failed to clear up; this number included all those cases in which the paraplegia was due to some sort of mechanical accident, and probably a few in which the cause was an abscess, early evacuation of which would have led to recovery. In no less than 96 cases (50%) the paraplegia was of late onset; in well over half (58 out of 96) recovery occurred spontaneously.

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On examination, she presented the picture of a spastic left hemiparesis, with atrophy of the small muscles of the hand, a right hemi-analgesia and thermohypæsthesia—indicating impaired conduction in the left spinothalamic tract—and proprioceptive loss distally in the limbs, more marked on the left side. X-ray films showed that the tip of the odontoid process was in contact with the posterior arch of the atlas and that the displacement had also been fortunately off to one side, so that the odontoid had gradually slipped forwards and to the left and was indenting the left lateral aspect of the cord. This asymmetrical luxation was later proved to be due to yielding of the atlanto-axial articulation on the left side only, due to a tuberculous synovitis. The corresponding joint on the right side was healthy and had stood firm. The lateral view showed a small focus of osseous tuberculosis anteriorly in the body of the axis.

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The natural curvature of rib conformed well to this part of the skeleton.

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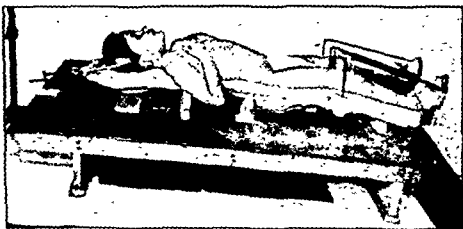


FIG. 1.—Posterior plaster shell, carrying post for attachment of skull-traction appliance.



FIG. 2.—Anterior shell applied preparatory to turning; skull-traction transferred to post on anterior shell.



FIG. 3.—Detail of the detachable posts and rubber tubes to prevent foot-drop while preserving a range of movement.

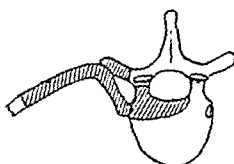


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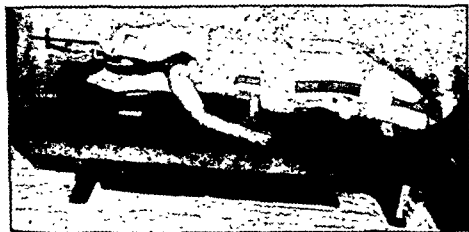


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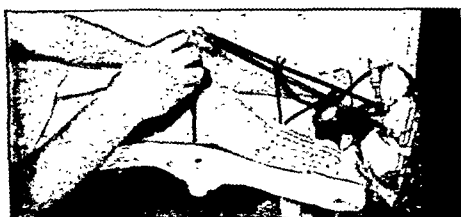


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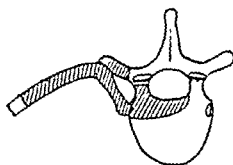


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Mr. Dott and I have been using a lateral approach to the diseased region in the past eighteen months, and the series to date amounts to 13 cases. This method affords an excellent visualization of the contents of the vertebral canal and has been notably revealing in regard to the morbid anatomy. It provides access to the anterior aspect of the theca and, as will be seen, this is so important that we have called it an antero-lateral decompression. The neurological recovery following this operation has been so satisfactory and rapid that we are encouraged to persevere with it. It must be emphasized, however, that the operation is still on trial and undergoing modification.

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The antero-lateral decompression operation is in large part an extensive costo-transversectomy but goes further. The skin incision is curved, commencing and terminating at the mid-line well above and below the region of the spine to be exposed, forming a crescentic flap extending three or four inches from the mid-line at the level of disease. Trapezius and/or latissimus dorsi are incised just lateral to the spinous processes, where the muscles are still relatively aponeurotic. These flat muscles are displaced laterally. The longitudinal posterior muscles are then reflected medially exposing the angles of the ribs. A generous resection of three or more ribs is made, going two or three inches lateral to the angles and as far medially as possible with rib shears. The transverse processes and neck and head of ribs are then nibbled away. Intercostal nerves are now apparent and we have found them an important guide in locating the pedicles and theca. By this stage, one is often working among diseased soft tissues and necrotic bone, with much anatomical deformity and the intercostal nerves are about the only reliable structures on which to rely.

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The theca below the gibbus shows none of the natural systolic pulsation but on removal of the compressing agent the theca falls forward and in our experience in most cases pulsation has then been evident throughout the whole length exposed. In a few cases no such pulsation reappeared although lumbar manometry after operation was satisfactory and subsequent recovery complete. At the conclusion of the operation one sees the arched theca, probably pulsating naturally, with the now lax intercostal nerves emerging in series, and disposed across the deeper part of the wound like the legs of a spider. The work on the gibbus is, of course, conducted between these nerves, retracted upwards or downwards with a loop of thread as convenient.

It will be evident that kyphosis materially assists access to the lateral aspect of the spinal column, and indeed when the gibbus is marked a full lateral view of the compressed theca is obtained at operation.

The operation is conducted on the anterior shell and we are now applying skull-traction as a preliminary step in the operation in cases with involvement of upper thoracic vertebrae. The patient is placed in the posterior shell about fifteen days after operation when wound healing is well under way. Professor Albert of Liège on a recent visit to us remarked that he has observed no ill-effect from using the posterior shell immediately after spinal

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In every one of the 13 cases operated on so far some gross mechanical factor was found to account for the spinal cord compression and in all instances pressure was being exerted mainly upon the anterior aspect of the theca and cord.

In 7 instances one or more intervertebral discs at the diseased level, usually at the apex of the gibbus, were displaced backwards and were grossly indenting the theca anteriorly. A sequestrum similarly displaced posteriorly was responsible in 2 cases, and in 2 others a vertebral abscess bulged backwards. In conformity with the wedge-shaped focus of disease it is natural that loose discs and sequestra should pass backwards when kyphosis has developed, and so come to lie hard up against the theca and cord. Two cases of the series, examples of "late paraplegia", were healed but presented a transverse ridge of bone indenting the theca at the level of the gibbus.

The removal of discs and sequestra is easy but healed cases are apt to present technical problems calling for patience and finesse if hard bone is to be removed without detriment to the cord. We believe that persistent discs and sequestra probably impede re-ossification in continuity at the diseased level, and if so their removal would seem a logical step. Time will provide an answer and it is quite possible that one of the standard bone-grafting procedures will later be required.

The indications for decompression of the cord in Pott's disease are we think no different from those in cord-compression from other causes. One cannot ignore the threat of irrevocable ischemic damage to the cord in cases with severe and rapid development of the compression syndrome. This state of affairs calls for prompt action. Then there is the type of case in which the compression of the cord persists or advances in spite of adequate extension and fixation, and we think that in such cases the wait-and-see policy is questionable.

In passing I should like to sound a warning against the assumption that a good response in the lumbar manometer and low protein content in the lumbar C.S.F. are evidence against the existence of compression of the cord. It should be recognized that if the theca is flattened anteriorly fluid may find its way readily enough past the cord laterally at the level of compression. This was observed in one case in this series, and is, of course, also quite common in cervical disc-protrusion implicating the cord and in some extramedullary spinal tumours. The neurological status and progress are more important indications of what is going on within the vertebral canal.

The neurological recovery following the operation described can at times be dramatic and we have twice observed a substantial return of voluntary movement to the completely paraplegic lower limbs as early as twelve hours after operation. With one exception all cases have recovered complete or almost complete motor and sensory function. The exception refers to an adult with healed-extreme kyphosis exceeding a right-angle, dating from early childhood, with paraparesis of late onset. The spinal cord was like a ribbon, stretched across a transverse ridge of bone at the apex of the gibbus. The greatest caution was exercised in avoiding disturbance of the cord, nevertheless the melancholy result has been that of a total transverse lesion. One spinal branch of an intercostal artery opposite the gibbus was damaged during exposure and it is highly probable that this was an artery of importance in the segmental supply to the cord. The lesson is obvious.

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In every one of the 13 cases operated on so far some gross mechanical factor was found to account for the spinal cord compression and in all instances pressure was being exerted mainly upon the anterior aspect of the theca and cord.

In 7 instances one or more intervertebral discs at the diseased level, usually at the apex of the gibbus, were displaced backwards and were grossly indenting the theca anteriorly. A sequestrum similarly displaced posteriorly was responsible in 2 cases, and in 2 others a vertebral abscess bulged backwards. In conformity with the wedge-shaped focus of disease it is natural that loose discs and sequestra should pass backwards when kyphosis has developed, and so come to lie hard up against the theca and cord. Two cases of the series, examples of "late paraplegia", were healed but presented a transverse ridge of bone indenting the theca at the level of the gibbus.

The removal of discs and sequestra is easy but healed cases are apt to present technical problems calling for patience and finesse if hard bone is to be removed without detriment to the cord. We believe that persistent discs and sequestra probably impede re-ossification in continuity at the diseased level, and if so their removal would seem a logical step. Time will provide an answer and it is quite possible that one of the standard bone-grafting procedures will later be required.

The indications for decompression of the cord in Pott's disease are we think no different from those in cord-compression from other causes. One cannot ignore the threat of irrevocable ischæmic damage to the cord in cases with severe and rapid development of the compression syndrome. This state of affairs calls for prompt action. Then there is the type of case in which the compression of the cord persists or advances in spite of adequate extension and fixation, and we think that in such cases the wait-and-see policy is questionable.

In passing I should like to sound a warning against the assumption that a good response in the lumbar manometer and low protein content in the lumbar C.S.F. are evidence against the existence of compression of the cord. It should be recognized that if the theca is flattened anteriorly fluid may find its way readily enough past the cord laterally at the level of compression. This was observed in one case in this series, and is, of course, also quite common in cervical disc-protrusion implicating the cord and in some extramedullary spinal tumours. The neurological status and progress are more important indications of what is going on within the vertebral canal.

The neurological recovery following the operation described can at times be dramatic and we have twice observed a substantial return of voluntary movement to the completely paraplegic lower limbs as early as twelve hours after operation. With one exception all cases have recovered complete or almost complete motor and sensory function. The exception refers to an adult with healed extreme kyphosis exceeding a right-angle, dating from early childhood, with paraparesis of late onset. The spinal cord was like a ribbon, stretched across a transverse ridge of bone at the apex of the gibbus. The greatest caution was exercised in avoiding disturbance of the cord, nevertheless the melancholy result has been that of a total transverse lesion. One spinal branch of an intercostal artery opposite the gibbus was damaged during exposure and it is highly probable that this was an artery of importance in the segmental supply to the cord. The lesson is obvious.

Sex and age call for no special comment in the series; the youngest patient was aged 6 years, the oldest 65 years. The two patients with a healed lesion and late paraparesis were adults in the fourth decade.

Three of the 13 patients died, an operative mortality of 23%. They were all serious cases from the neurological point of view, with rapid onset of complete paraplegia. Two died of uremia three and four days after operation; in one of these military renal tuberculosis was found. We make it a practice now to assess renal efficiency and are unwilling to advise this rather formidable operation for the patient over 50 years of age unless the situation is one of extreme urgency. The third patient died ultimately from the effects of an unrelieved compression of the cord. This was one of the earlier cases and had a previous lateral decompression in which pedicles alone were removed, followed later by an antero-lateral decompression with approach from the opposite side. Thus pedicles were removed bilaterally and such instability resulted that intact vertebral bodies were soon over-riding. Had we been quicker in applying skull traction and in performing a stabilizing bone-graft the unfortunate outcome in this case might have been avoided. The lateral decompression was obviously ineffective and we abandoned it after this one experience. It formed, however, the link between costo-transversectomy and the antero-lateral decompression operation.

No evidence has so far been forthcoming that the operation disseminates infection. Although no clear evidence of sound re-ossification is yet to hand in this rather recent series, it can be said that the disease has not advanced, as judged radiologically, except in the case in which a sinus developed at the wound.

I am not in a position to speak from personal experience of the value of costo-transversectomy with evacuation of paravertebral abscess. Certainly that operation gives some good results and might well be considered for the case deemed unfit for the anterior decompression. In such circumstances, however, no substantial relief of pressure on the cord by say an intervertebral disc could be expected. Skull-traction would seem to have a place in the management of thoracic Pott's disease in this category, and very considerable traction and extension could be provided in the semi-sitting position, as described by McKenzie (1935) and more recently by Guthkelch (1945). We have not yet had occasion to use this method.

The following two cases are of clinical interest:

We have seen recently a boy of 12 years whose tuberculous kyphosis was precipitated quite definitely by the spasms of tetanus. Later he developed a spastic paraparesis but had recovered fully from this when we saw him. It had been thought that his rounded "juvenile kyphosis" was well ossified, and so it seemed on superficial examination of the X-ray films which came with him. Stereoscopic views showed what we had suspected, namely calcifications in a large paravertebral abscess overlying the extremely rarefied tuberculous vertebral bodies. This case exemplifies an unusual precipitating factor in the development of kyphosis in Pott's disease, and also emphasizes the value of stereoscopic X-ray films.

Another boy of 9 years, one of the anterior decompression series, exhibited a slight ataxia of one upper limb which was puzzling until we obtained films showing a large calcified tuberculoma in the cerebellum. The lesson here I suppose, is to be on the look-out for the occasional case with multiple foci of involvement of the nervous system.

A few final remarks may perhaps be permitted, as an epilogue, on a topic which though not embraced in the term paraplegia is of neurological interest in connexion with tuberculosis of the spine:

We have had two patients presenting superficially the syndrome of ruptured lumbar intervertebral disc. Both were young soldiers complaining of lumbar backache and of monoradicular type of referred sciatic pain, L5 in one case and S1 in the other. The backache dominated the picture and recurred after periods of rest more rapidly and constantly than is typical with ruptured intervertebral disc. X-ray examination disclosed a characteristic "woolliness" at one intervertebral space and localized subperiosteal erosion of adjacent anterior surface of vertebral bodies. One of the patients was operated on deliberately a year ago because of an exacerbation of the root-compression syndrome, and typical pus and tuberculous debris were evacuated from the lumbo-sacral space after the grossly bulging annulus had been incised. The root pain promptly ceased. Incidentally his progress in a sanatorium, immobilized in plaster, was giving every satisfaction when he died suddenly of a pulmonary embolus two months ago.

Pott's paraplegia presents a problem involving risk to the patient and very considerable labour on the part of medical and nursing personnel: it offers a field for improvement in management. The neurological complications of Pott's disease are often preventable and can be traced to faulty early diagnosis and to imperfections and delay in treatment when the disease has been diagnosed. One should look forward perhaps to a future in which the major operative procedure described in this paper will be of little more than historical interest.

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Section of Comparative Medicine

President—W. A. POOL, M.R.C.V.S.

[April 17, 1946]

DISCUSSION ON

LEUKÆMIA AND LEUKOSIS IN MAN AND ANIMALS

Professor J. Engelbreth-Holm: *The comparative pathology of animal leukosis.*—The comparative pathology of animal leukoses and their relationship to leukosis in man are subjects which seem perhaps even more difficult to deal with adequately to-day than appeared to be the case some years ago. We cannot, for instance, adequately define the term "leukosis" so as to exclude states similar to that morbid condition but in some ways different from it. The leukæmoid reactions in infections and intoxications occur in both man and animals. Then again, we are not sure whether the various conditions we consider to represent leukosis are all of similar nature: for instance, some of the lymphoid leukoses seem to behave differently from the more typical leukotic diseases.

Leukoses seem to me to be true malignant growths arising from the hæmopoietic tissues. They were at first believed to represent the reaction to infections and this view was then followed by the theory that they represented biologically benign hyperplasias. Our present view is that leukoses are neoplastic conditions exhibiting true autonomous growth. It is possible that certain leukotic states are due to metabolic disorders. It may well be that the leukoses include a variety of conditions of diverse origin. It would, in my view, be a valuable procedure to try to eliminate from the leukoses all conditions which do not conform to the definition "tumour growth of the blood-forming tissues". This is, however, a very difficult task.

The classification of true leukoses is itself a difficult problem. It was formerly the custom merely to classify leukosis according to the type of cell involved: myelogenous, erythroblastic, lymphogenous, monocytic or reticulocytic, and plasma cell (human pathology only). Within each of these types, however, the condition may manifest itself in different ways, displaying the features of acute or chronic leukosis which possibly are analogous to the varying stages of differentiation of the cells of malignant tumours in general. The classification into leukæmic and aleukæmic leukosis is of doubtful value.

There is some evidence from studies of leukosis in man and in the mouse which makes it doubtful whether a strict classification such as that outlined above is justifiable. For

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One can conclude that leukosis depends on the genetic constitution of the organism, a fact which stands out very clearly from work on the mouse and also from Dr. Videbæk's observations in man. Whether the influence of hormones and of caloric restriction is as marked in human leukosis as has been found in the mouse is not known, but it is known that in both species there occurs acceleration of leukosis in predisposed individuals by exogenous carcinogens. This has been shown in mouse leukosis for X-rays and carcinogenic hydrocarbons and in man for X-rays and radium. Attempts to cure mouse leukosis with the aim of finding suitable methods for human leukosis should be undertaken but the work should be carried out with the spontaneous disease since results with the transplanted disease in the mouse will be of more doubtful value.

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In spite of these reservations it is nevertheless advisable to treat each form of leukaemia separately, especially if we are to distinguish true leukaemia from allied morbid states of doubtful origin.

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For practical purposes we can regard this group of diseases as particularly contagious during early life and affecting principally fowls of certain breeding. Studies on avian leukaemia may also produce information of comparative interest. For instance, the observation by Asplin (1941) that the acute chick disease produced by the agent recovered from neurolymphomatosis is curable by sulphonamide drugs indicates that chemotherapeutic measures should be explored in all diseases of this kind.

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Dr. E. G. White: *Leukæmia in the dog*.—This disease has been known to veterinarians for many years as Hodgkin's or Pseudo-Hodgkin's disease, although it is quite different from the disease in man. The condition is characterized by great enlargement of the lymph nodes and nearly always of the spleen, and by leukæmic infiltration of various other organs and tissues. A recent detailed study of the disease in the United States (Bloom, F., and Meyer, L. M., 1945, *Amer. J. Path.*, **21**, 683-715), which included examination of the peripheral blood and bone-marrow biopsy, suggests the term "malignant lymphoma" for the disease and classifies it, according to the type of malignant cell, as lymphoblastic, lymphosarcoma-cell, mixed-cell, and lymphocytic.

Among 512 dogs coming to us for autopsy during 1938-39 the incidence was 1.8%. The incidence among dogs coming to clinics is about 0.1—0.3%. Only 2 of 44 cases occurred in animals under 3 years old, and the highest incidence was between 4 and 8 years. Although a total of 21 breeds were represented in the series there were 10 cases in Aberdeen Terriers and it is of interest that the incidence in this breed was high in the series examined by the American workers quoted above. The clinical history was of enlargement of the lymph nodes of the throat and neck for one to four weeks before admission. All the animals had either died or had been destroyed *in extremis* within nine weeks of admission. Considerably longer periods of survival have been recorded in the literature, however. Almost all the lymph nodes are eventually grossly enlarged, the spleen is readily palpated, there is often diarrhoea and sometimes a cough, and wasting is considerable. Enlargement of the lymph nodes of the throat may cause local oedema and this was sometimes the reason for having the animal destroyed.

The blood shows anæmia and usually a high leucocyte count but the latter is mainly due to an excess of neutrophil leucocytes, including many non-segmented cells and occasional myelocytes. The American workers consider the blood picture to indicate a neutrophil leucocytosis and in some animals they found widespread extramedullary myelopoiesis, which, in the past, has sometimes given rise to the mistaken diagnosis of myeloid leukaemia. It is doubtful whether true myeloid leukaemia has been recorded in the dog.

Three cases of the disease were treated with urethane by Mr. G. C. Knight, at Dr. Haddow's suggestion, but although there was, at first, some improvement of the general condition the lymph nodes remained enlarged and the disease later progressed as in untreated animals.

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To summarize the results achieved by comparative studies of the pathology of leukaemia we may say that our classification is unsatisfactory. We need to separate leukaemic reactions following infections and also myelosclerosis from the group of true leukaemias. We should also consider whether we need a special group to include cattle leukaemia, chronic lymphatic leukaemia in aged people, and perhaps also non-transmissible lymphogenous leukaemia of fowls. We have also seen that true leukaemias are malignant tumours of the haemopoietic tissues and are analogous in animals and man, and also that morphologically different types occur, due to varying genetic factors and are not to be considered as being so widely separated as hitherto.

Mr. F. Blakemore: Avian leukaemia.—This group of diseases is of enormous economic importance to the poultry industry. Ellerman's original classification of fowl leukaemia into myeloid, erythroid and lymphoid forms, has held good in principle, but a certain amount of confusion has arisen regarding the relationship between these conditions. The occurrence of lymphomatosis during recent years has complicated the position still further. There is now evidence that erythroleucosis and myeloid leukaemia are closely related (Stubbs and Furth, 1931) and they may occur as different manifestations of the same infection. The position regarding lymphatic leukaemia remains unsettled; it was originally believed to be non-transmissible but now some workers do not recognize it as a specific entity and regard it as a manifestation of lymphomatosis. It seems probable, however, that it can occur as a separate condition and some cases may arise from infection with a lymphoid tumour agent similar to that described by Olsen (1941).

There is a lack of agreement regarding the relationship between lymphomatosis, both visceral and neural, and the true leukaemic conditions. The occurrence of all forms of leukaemic disease, in groups of fowls inoculated with material from a single donor affected with lymphomatosis, has led to the so-called "unitarian theory" (Biester and Devries, 1944) which attributes them to a single virus, and classifies them together as the "leucosis complex". Further information regarding the correctness of this theory is desirable, since the evidence on which it is based is open to the criticism that experiments have not been carried out with virus-free stocks.

Neurolymphomatosis (fowl paralysis) is much more prevalent in this country than the true leukaemic conditions, which tend to be sporadic. It differs from true leukaemia in that there is no significant blood change. The lesions vary from a slight diffuse infiltration of certain organs to single or multiple lymphomatous tumours in the viscera.

The peripheral nerves are often also infiltrated although nerve lesions may be a manifestation of certain other transmissible conditions of the fowl (Furth, 1935). In a pathological sense neurolymphomatosis probably occupies an intermediate position between the inflammatory conditions and those which are characterized solely by an unrestricted autonomous proliferation of blood elements. Like the leukaemic conditions it also resembles, in some respects, the neoplastic conditions.

It is now generally agreed that avian leukaemia is due to virus infection. My own experiences have been mainly limited to the agent recovered from neuro-lymphomatosis and its properties can be summarized as follows:

(1) Neurolymphomatosis virus is much more infective to chicks than older stock; the resistance factor develops gradually and cannot be attributed to previous infection.

(2) While the natural disease is essentially chronic and rarely manifested under the age of 5 months, the virus can be raised in virulence by rapid passage through groups of chickens. In this state it causes a disease which is fatal within a few days.

(3) The rise in virulence of the lymphomatosis virus is accompanied by a marked change in the effect it produces on the tissues, the acute disease being characterized by necrosis of the capillary walls and cells in their immediate vicinity. In this respect there is a similarity between it and the Rous sarcoma virus which Duran-Reynals (1940) described as producing an acute haemorrhagic disease in young chicks.

(4) Another point of resemblance between these two agents is the varying susceptibility of different strains of fowls to infection. Some strains of chickens are particularly resistant to the agent recovered from lymphomatosis. Only some of the susceptible strains, and certain individuals of these strains, develop proliferative lymphocytic lesions as a manifestation of chronic infection. The possibility that two agents are concerned in the aetiology of this neoplastic kind of response has been considered, since it seemed possible that the lymphomatosis virus may play the rôle of an agent exciting a second latent infection carried by certain fowls. We have been unable, however, to obtain

any positive evidence that this is the explanation of the difference in behaviour between susceptible fowls.

For practical purposes we can regard this group of diseases as particularly contagious during early life and affecting principally fowls of certain breeding. Studies on avian leukaemia may also produce information of comparative interest. For instance, the observation by Asplin (1941) that the acute chick disease produced by the agent recovered from neurolymphomatosis is curable by sulphonamide drugs indicates that chemotherapeutic measures should be explored in all diseases of this kind.

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Dr. R. J. Ludford raised the question whether the sensitivity of leukaemia cells was related to the frequency of mitosis. Professor A. P. Dustin had often drawn attention to the fact that the lymphoid tissues were specially sensitive to his "poisons caryoclasiques", which included a variety of chemical compounds and ionizing radiations. Then Lits, Kirschbaum and Strong reported that a rapidly growing lymphoid mouse tumour with which they worked was extremely sensitive to the mitotic poison, colchicine. Some tumours appeared to regress completely after treatment but always recurred so that the mice died ultimately of leukaemia. While it is generally true that the more rapid the growth of cells, the more readily they are injured by toxic substances, nevertheless cells of different tissues exhibit different susceptibility to poisons. There is the possibility that the relatively small mass of cytoplasm in proportion to nuclear volume renders cells of the lymphocyte type particularly sensitive to injury by physical and chemical agents.

Professor G. R. Cameron asked Professor Engelbreth-Holm whether he had any explanation for the numerous hæmorrhages which so commonly accompany the more acute forms of leukaemia. He had frequently examined such hæmorrhages by means of serial sections and was unable to come to any conclusion as to their nature. Rupture of vessels could not be established. Capillaries were most frequently a site of bleeding, and it was difficult to associate any structural change in them with the extravasations of blood.

He also inquired whether Professor Engelbreth-Holm had any information about the action of nitrogen mustards in leukaemia. Some of these compounds were water soluble, and could be made suitable for administration; in fact, some work had already been done in America. The nitrogen mustards, like the classical sulphur-containing mustard gas, have a specific destructive action on the granulocyte-forming tissue of the bone-marrow, as well as on the lymphoid tissue. It was possible to lower the white cell content of the blood by means of small doses without any grave disturbance of other tissues. The effects were temporary, however, and there was no evidence of maintained improvement. A great deal more research work needed to be done on this subject and it might be possible by means of co-operation between the chemist and the clinician, to obtain a potent compound which was safe and exerted the minimal harmful effects.

Dr. L. Foulds agreed with previous speakers about the difficulties in the diagnosis and classification of the leukoses and referred to transitional forms between typical leukoses and typical neoplasms in fowls.

Professor Engelbreth-Holm in reply to Dr. J. M. Alston: The problem of how aleukæmic leukaemia is to be understood is rather obscure. I do not think that it is necessary to assume a double failure of function. We have to wait for further information whether the suggestion of Rohr is right. Rohr is of the opinion that aleukæmic leukaemia occurs when the leukæmic processes are restricted to the bone-marrow, whereas the leukæmic picture will only develop in those cases where leukæmic processes are found outside the skeleton (spleen, liver, &c.). I am not convinced myself that this suggestion is correct, but Dr. C. Johansen in Copenhagen, in an exclusive work not yet published, thinks that Rohr is right.

As to the ætiology of leukaemia the view of Gohs was put forward by Dr. Rothe Meyer and myself in 1933. "The lytic substance" is obviously nothing but the virus in fowl leukaemia and this hypothesis only concerns fowl leukaemia and Rous sarcoma.

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I have no experience of the action of nitrogen mustard.

Section of Urology

President—A. WILFRID ADAMS, M.S.

[February 28, 1946]

The Female Urethra and its Relation to Upper Urinary Tract Infections. [*Abridged*]

By HOWARD G. HANLEY, M.D., F.R.C.S.

THE main purpose of this paper is to attempt to demonstrate the close relationship between urethral inflammation and upper urinary tract infection in women of the child-bearing age.

Over half of the women attending my genito-urinary clinic have symptoms directly referable to the urethra and I find it difficult to explain the general lack of attention shown to this organ in this country. The standard British textbooks of medicine, surgery and gynaecology hardly mention inflammatory lesions in the female urethra other than caruncles or gonorrhœa; not that the symptoms of frequency, urgency and dysuria, are neglected, far from it, but they are generally ascribed to cystitis which I contend is a relatively rare condition compared with the urethro-trigonitis which really causes these symptoms. The work and papers of Folsom in 1931, and later of Stevens (1935) and Bugbee (1917) and many others have received recognition in America, and the fact that the female urethra is a common source of symptoms is accepted in that country, but here in England apart from the late Frank Kidd, Winsbury-White (1933*a*) has been a voice crying in the wilderness on this subject for many years.

Two simple groups of inflammation can occur in the female urethra—the purulent and the non-purulent. The purulent form is commonly, but not only, due to the gonococcus and is recognized by everyone; but the non-purulent type, particularly if associated with a normal urine as frequently happens, is not only seldom diagnosed but its existence is even denied by some surgeons.

It is this non-purulent urethritis, or, as it is sometimes called, granular-urethritis or cystalgia (Ormond, 1935) with which I am concerned here.

The pathology is really a urethro-trigonitis, and although this is essentially a chronic disease, the onset is generally acute and there may be acute exacerbations. The acute onset, or any one of the acute exacerbations may progress to a typical pyelitis—a point which I would stress. When a case of acute urethro-trigonitis is seen immediately it develops, it is impossible to estimate whether it will become a pyelitis or not, since the symptoms of both conditions in the first twenty-four to forty-eight hours are identical in a majority of cases. 54% of the women in the pyelitis group to be reviewed later, gave a history of a urethro-trigonitis preceding the onset of their pyelitis.

Acute urethro-trigonitis.—In the majority of women the initial onset of urethro-trigonitis is sudden; they are seized with urethral pain and an urgent desire to micturate. The actual passage of urine is extremely painful and even when the bladder is emptied

Dr. R. J. Ludford raised the question whether the sensitivity of leukaemia cells was related to the frequency of mitosis. Professor A. P. Dustin had often drawn attention to the fact that the lymphoid tissues were specially sensitive to his "poisons caryoclastiques", which included a variety of chemical compounds and ionizing radiations. Then Lits, Kirschbaum and Strong reported that a rapidly growing lymphoid mouse tumour with which they worked was extremely sensitive to the mitotic poison, colchicine. Some tumours appeared to regress completely after treatment but always recurred so that the mice died ultimately of leukaemia. While it is generally true that the more rapid the growth of cells, the more readily they are injured by toxic substances, nevertheless cells of different tissues exhibit different susceptibility to poisons. There is the possibility that the relatively small mass of cytoplasm in proportion to nuclear volume renders cells of the lymphocyte type particularly sensitive to injury by physical and chemical agents.

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3% of the group gave a history of a previous abortion, and most of these were eight to ten years before, although one woman stated that her symptoms began after a dilatation and curettage two years previously. Under 1% of the pyelitis cases had had an abortion within three months of their pyelitis. I would say that the case against abortion is non-proven.

In the same way, normal childbirth would not seem to be an important ætiological factor. As one would expect, the majority of women in this age-group are married, but although many women say they were perfectly well before they became pregnant, the percentage of childless women (53%) is extraordinarily high.

The next generalization was the surprisingly low incidence of accompanying pelvic pathology other than cervical erosion; this latter undoubtedly has a very close relationship to urethral inflammation. While agreeing that gross pelvic pathology must always be corrected in women suffering from urinary symptoms, it is important to remember that cystocele *per se* is not a common cause of such symptoms.

The physical examination of these patients may therefore reveal no abnormality at all and a catheter specimen of urine is next obtained; here, of course, lies another trap, since although the urine *may* contain red blood corpuscles, pus cells and *B. coli*, it is usually crystal clear, contains no deposits and may even be sterile on culture; this fact has caused many surgeons to lose interest in these cases since they argue that no inflammatory pathology can be present if the urine is clear and sterile. If these women are cystoscoped in the lithotomy position so that the vulva can be carefully inspected, it will be noted that in the more acute cases the urethral orifice is frequently oedematous and hyperæmic, but that in the long-standing cases there is no apparent pathological condition. Only three instances of caruncle occurred in this whole series. However, narrowing of the urethral lumen is one of the commonest findings and it should come as no surprise if a 22 Charrière cystoscope cannot be introduced into the bladder. Many authors have now commented on this phenomenon, especially Stevens and Winsbury-White who consider that a urethral lumen which will not admit a 26 French sound is contracted. Urethral dilatation may be necessary therefore before cystoscopy can be performed. The cystoscopic findings in these cases vary but in the great majority of them the bladder shows the normal pinky yellow colour, while the ureteric orifice and the trigone may be normal as well. Symptoms in these women lead one to make a diagnosis of cystitis which is disproved time and time again by cystoscopy, and I feel that in general a diagnosis of cystitis is made far too loosely; as a primary lesion it is a rare condition. A localized trigonitis, however, is commonly associated with this syndrome. At times it may only involve the front of the trigone near the urethral orifice or it may run up along the area of one of Mercier's bars towards the ureteric orifice. Again, it may be absent altogether, but one thing is definite, it is never present without a similar or worse degree of pathology in the urethra and this would indicate that the inflammation commences in the urethra and spreads back to the trigone in most cases.

In seeking a cause for these women's symptoms a rapid routine cystoscopy may, therefore, reveal no abnormality and it is not until the instrument is withdrawn to show the margin of the internal urethral orifice that signs of pathology are evident. A collar of large congested vessels may be seen but the surest sign of trouble is the presence of oedematous, translucent, pedunculated or sessile polypi. It may only be possible to see these structures by holding the cystoscope obliquely so that it makes an angle of nearly 45 degrees with the axis of the urethra. A foroblique telescope is much better for the purpose but, of course, the urethroscope is the ideal instrument. These polypi appear singly or in clusters, usually between 10 and 2 o'clock, some are solid, rigid hillocks (an excellent term used by Winsbury-White, 1939), others are pedunculated and translucent and may burst when the beak of the instrument is pressed on them, and certainly if touched with the diathermy current.

Much research has been done on these polypi or hyperplastic changes as they have been termed (Hyams, 1944). Some workers think they are glands analogous to the male structure while others deny that there are glands in the female urethra, but all agree that they are pathological. I have removed several of the larger polypi with the cold punch, but the sections merely show evidence of chronic inflammation in a fibrous tissue matrix. No gland tissue has been seen.

Symptoms in relation to clinical findings.—These hyperplastic urethral changes are found so often in association with the symptoms of frequency and dysuria, &c. that there can be little doubt they are a part of the syndrome. However, although the clinical

the desire persists, and patients have reported how they were forced to sit on the lavatory for hours on end passing only a few drops of urine at a time. Terminal hæmaturia is common at this stage. Sometimes dysuria is present without any frequency at all, particularly in young women who say that they can hold their urine for four to five hours with comfort, but are afraid to micturate. Under such conditions acute retention may easily develop.

The acute symptoms which are associated with very marked constitutional effects, may last for several days, perhaps being severe enough to confine the patient to bed, but more usually the whole picture is less severe and the symptoms have completely subsided in a week or so. Mostly these acute cases are seen and treated by the general practitioner as "cystitis" and if they subside rapidly they never reach the out-patient department.

During the acute stage the urine may be infected with *B. coli* and contain pus and red cells, but it is surprising how quickly it will clear completely in some cases while the symptoms will remain. Cystoscopy performed very shortly after the acute phase may reveal no abnormality in the bladder mucosa at all, but the trigone and urethra are nearly always inflamed. The urethroscopic findings are, however, very transient and there may be nothing abnormal to see after a week or so. It is not until a chronic state develops that gross findings become common.

Chronic urethro-trigonitis.—A high proportion of cases settle down into a state of chronic urethral irritability, which, punctuated by acute exacerbations, may go on for months or years before the surgeon sees them, unless they develop an attack of pyelitis. The symptoms in these women are primarily frequency and dysuria, the frequency often being worse in the morning than later in the day, and although nocturia is common, it is never as severe as in tuberculous cases and may be absent altogether. Dysuria of a burning nature usually precedes or follows, though it may accompany the act. Sometimes dysuria is present without any frequency at all, particularly in young women, where pain or discomfort long after micturation may be the sole symptom. On the other hand the dysuria is often associated with urgency or precipitancy which may be so acute as to produce actual incontinence. A feeling of incomplete emptying of the bladder, suprapubic pressure and attacks of terminal hæmaturia are common findings.

Folsom (1934) and Winsbury-White (1933*a*) have both drawn attention to referred pain from the female urethra, such as pain in the loin, groin, thigh or suprapubic region. Folsom describes the special iliac type where multiple abdominal operations have usually been performed without relief. We must all have seen such cases. Personally I believe that many of these pains are due to an associated ureteritis. It is a surprising fact that women will put up with such symptoms for years on end before seeking advice.

The clinical data for this paper has been derived from a study of 433 women of the child-bearing age (15 to 47 years), who complained of some, or most, of the urethral symptoms already referred to, or who were admitted with pyelitis. Apart from a general systemic and a careful gynaecological examination, a full urological investigation was made in every case; this latter included microscopy and generally culture of the urine, cystoscopy and urethroscopy and in many cases excretion pyelography. It must be emphasized at this stage that it may be impossible to demonstrate the true urethral pathology by cystoscopy alone and the urethroscope, preferably an irrigating instrument such as the Geiringer or Swift Joly is essential.

The total number of patients with evidence of urethritis was 310, 132 having an associated pyelitis as well. A noticeable feature was that more than half of them had suffered their symptoms for a year or more while most of them had received medicinal treatment from their private doctors with varying degrees of relief, but the symptoms had quickly returned. The histories in some cases went back eight to ten years, exacerbations being treated with alkalies, &c.

The age distribution is, I think, important. 72% (35+37) of the 187 urethro-trigonitis cases were evenly distributed between the 21-30 and 31-40 age-groups. However, a detailed analysis of these women showed that the first onset of urethral symptoms dated back to the 21-30 age-groups in 48%, so that the chronic cases tend to be seen in the 31-40 age-group.

63% of the pyelitis cases occurred in the 21-30 age-group, at an age in fact when acute urethro-trigonitis is commonest.

Incomplete abortion has always been given as a frequent cause of urinary infection, but its role as an ætiological factor in urethro-trigonitis is not very convincing. Only

3% of the group gave a history of a previous abortion, and most of these were eight to ten years before, although one woman stated that her symptoms began after a dilatation and curettage two years previously. Under 1% of the pyelitis cases had had an abortion within three months of their pyelitis. I would say that the case against abortion is non-proven.

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The physical examination of these patients may therefore reveal no abnormality at all and a catheter specimen of urine is next obtained; here, of course, lies another trap, since although the urine may contain red blood corpuscles, pus cells and *B. coli*, it is usually crystal clear, contains no deposits and may even be sterile on culture; this fact has caused many surgeons to lose interest in these cases since they argue that no inflammatory pathology can be present if the urine is clear and sterile. If these women are cystoscoped in the lithotomy position so that the vulva can be carefully inspected, it will be noted that in the more acute cases the urethral orifice is frequently œdematous and hyperæmic, but that in the long-standing cases there is no apparent pathological condition. Only three instances of caruncle occurred in this whole series. However, narrowing of the urethral lumen is one of the commonest findings and it should come as no surprise if a 22 Charrière cystoscope cannot be introduced into the bladder. Many authors have now commented on this phenomenon, especially Stevens and Winsbury-White who consider that a urethral lumen which will not admit a 26 French sound is contracted. Urethral dilatation may be necessary therefore before cystoscopy can be performed. The cystoscopic findings in these cases vary but in the great majority of them the bladder shows the normal pinky yellow colour, while the ureteric orifice and the trigone may be normal as well. Symptoms in these women lead one to make a diagnosis of cystitis which is disproved time and time again by cystoscopy, and I feel that in general a diagnosis of cystitis is made far too loosely; as a primary lesion it is a rare condition. A localized trigonitis, however, is commonly associated with this syndrome. At times it may only involve the front of the trigone near the urethral orifice or it may run up along the area of one of Mercier's bars towards the ureteric orifice. Again, it may be absent altogether, but one thing is definite, it is never present without a similar or worse degree of pathology in the urethra and this would indicate that the inflammation commences in the urethra and spreads back to the trigone in most cases.

In seeking a cause for these women's symptoms a rapid routine cystoscopy may, therefore, reveal no abnormality and it is not until the instrument is withdrawn to show the margin of the internal urethral orifice that signs of pathology are evident. A collar of large congested vessels may be seen but the surest sign of trouble is the presence of œdematous, translucent, pedunculated or sessile polypi. It may only be possible to see these structures by holding the cystoscope obliquely so that it makes an angle of nearly 45 degrees with the axis of the urethra. A foroblique telescope is much better for the purpose but, of course, the urethroscope is the ideal instrument. These polypi appear singly or in clusters, usually between 10 and 2 o'clock, some are solid, rigid hillocks (an excellent term used by Winsbury-White, 1939), others are pedunculated and translucent and may burst when the beak of the instrument is pressed on them, and certainly if touched with the diathermy current.

Much research has been done on these polypi or hyperplastic changes as they have been termed (Hyams, 1944). Some workers think they are glands analogous to the male structure while others deny that there are glands in the female urethra, but all agree that they are pathological. I have removed several of the larger polypi with the cold punch, but the sections merely show evidence of chronic inflammation in a fibrous tissue matrix. No gland tissue has been seen.

Symptoms in relation to clinical findings.—These hyperplastic urethral changes are found so often in association with the symptoms of frequency and dysuria, &c. that there can be little doubt they are a part of the syndrome. However, although the clinical

the desire persists, and patients have reported how they were forced to sit on the lavatory for hours on end passing only a few drops of urine at a time. Terminal hæmaturia is common at this stage. Sometimes dysuria is present without any frequency at all, particularly in young women who say that they can hold their urine for four to five hours with comfort, but are afraid to micturate. Under such conditions acute retention may easily develop.

The acute symptoms which are associated with very marked constitutional effects, may last for several days, perhaps being severe enough to confine the patient to bed, but more usually the whole picture is less severe and the symptoms have completely subsided in a week or so. Mostly these acute cases are seen and treated by the general practitioner as "cystitis" and if they subside rapidly they never reach the out-patient department.

During the acute stage the urine may be infected with *B. coli* and contain pus and red cells, but it is surprising how quickly it will clear completely in some cases while the symptoms will remain. Cystoscopy performed very shortly after the acute phase may reveal no abnormality in the bladder mucosa at all, but the trigone and urethra are nearly always inflamed. The urethroscopic findings are, however, very transient and there may be nothing abnormal to see after a week or so. It is not until a chronic state develops that gross findings become common.

Chronic urethro-trigonitis.—A high proportion of cases settle down into a state of chronic urethral irritability, which, punctuated by acute exacerbations, may go on for months or years before the surgeon sees them, unless they develop an attack of pyelitis. The symptoms in these women are primarily frequency and dysuria, the frequency often being worse in the morning than later in the day, and although nocturia is common, it is never as severe as in tuberculous cases and may be absent altogether. Dysuria of a burning nature usually precedes or follows, though it may accompany the act. Sometimes dysuria is present without any frequency at all, particularly in young women, where pain or discomfort long after micturation may be the sole symptom. On the other hand the dysuria is often associated with urgency or precipitancy which may be so acute as to produce actual incontinence. A feeling of incomplete emptying of the bladder, suprapubic pressure and attacks of terminal hæmaturia are common findings.

Folsom (1934) and Winsbury-White (1933a) have both drawn attention to referred pain from the female urethra, such as pain in the loin, groin, thigh or suprapubic region. Folsom describes the special iliac type where multiple abdominal operations have usually been performed without relief. We must all have seen such cases. Personally I believe that many of these pains are due to an associated ureteritis. It is a surprising fact that women will put up with such symptoms for years on end before seeking advice.

The clinical data for this paper has been derived from a study of 433 women of the child-bearing age (15 to 47 years), who complained of some, or most, of the urethral symptoms already referred to, or who were admitted with pyelitis. Apart from a general systemic and a careful gynaecological examination, a full urological investigation was made in every case; this latter included microscopy and generally culture of the urine, cystoscopy and urethroscopy and in many cases excretion pyelography. It must be emphasized at this stage that it may be impossible to demonstrate the true urethral pathology by cystoscopy alone and the urethroscope, preferably an irrigating instrument such as the Geiringer or Swift Joly is essential.

The total number of patients with evidence of urethritis was 310, 132 having an associated pyelitis as well. A noticeable feature was that more than half of them had suffered their symptoms for a year or more while most of them had received medicinal treatment from their private doctors with varying degrees of relief, but the symptoms had quickly returned. The histories in some cases went back eight to ten years, exacerbations being treated with alkalies, &c.

The age distribution is, I think, important. 72% (35+37) of the 187 urethro-trigonitis cases were evenly distributed between the 21-30 and 31-40 age-groups. However, a detailed analysis of these women showed that the first onset of urethral symptoms dated back to the 21-30 age-groups in 48%, so that the chronic cases tend to be seen in the 31-40 age-group.

63% of the pyelitis cases occurred in the 21-30 age-group, at an age in fact when acute urethro-trigonitis is commonest.

Incomplete abortion has always been given as a frequent cause of urinary infection, but its role as an ætiological factor in urethro-trigonitis is not very convincing. Only

3% of the group gave a history of a previous abortion, and most of these were eight to ten years before, although one woman stated that her symptoms began after a dilatation and curettage two years previously. Under 1% of the pyelitis cases had had an abortion within three months of their pyelitis. I would say that the case against abortion is non-proven.

In the same way, normal childbirth would not seem to be an important aetiological factor. As one would expect, the majority of women in this age-group are married, but although many women say they were perfectly well before they became pregnant, the percentage of childless women (53%) is extraordinarily high.

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evidence and the papers of many workers support this assumption, I have heard it argued that since these urethral findings are so common they can be of no significance. It is obviously a very important point and it was therefore decided to examine the urethra of a control series of women of the same age-group who had never at any time complained of any symptoms of abnormal micturition. The selection was rigid in that micturition by day must not be oftener than three-hourly, no nocturia, dysuria, scalding urgency or stress incontinence was allowable, and there had to be no previous attack of cystitis or pyelitis during childhood or pregnancy, or particularly following marriage. The results of this investigation are interesting. Before a series of 70 women with abnormal symptoms could be collected, over 200 women had to be questioned closely, i.e. 2 in every 3 women gave a history of some previous disturbance of micturition. In the average parous woman, nocturia would appear to be the rule, while urgency and day frequency at hourly intervals are not unusual. This shows the high incidence of minor degrees of urogenital pathology and is surely a reflection on our profession for taking so little interest in it. The 70 symptomless, normal women were admitted to hospital for various conditions such as interval appendicectomy, herniotomy, incomplete abortions, minor orthopaedic lesions, &c., and they were all urethroscopied under general anaesthesia; the urines in every case were normal. A further 19 random controls were selected for urethroscopy who, although they were not suffering from any urinary symptoms at the time, did give a history of previous attacks of cysto-urethritis.

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Urethral polypi and hillocks were present in 5 of the 70 controls, but all of these women were cases of abortions or salpingitis. Nothing pathological was found in women suffering from non-genital lesions. Of the 19 women symptomless at the time but having a previous urinary history, 13 or 68% showed evidence of urethral pathology. 70% of these 89 women were married and the only single woman to show any urethral changes was recovering from a salpingitis.

These figures do at least suggest that urethral polypi and hillocks are rare in previously uninfected urethra, and that when present they do probably indicate an inflammatory condition.

Mode of infection.—A careful history is most instructive and revealing in these women. The first symptoms date from the time of marriage in so many cases that there can be no doubt whatever that the sexual organs are very closely bound up with the aetiology of the condition. The first onset of urethral symptoms developed within three months of marriage in 80% of the women in the series. In 10% symptoms developed immediately after marriage and were duly recognized as so-called "honeymoon" cystitis. On the other hand, it is not only defecation which precipitates the attack; coitus after a prolonged interval appears equally to blame and numerous women who have been married for years and even borne children, complained of their first attack during their husband's leave from the Services.

Lymphatic spread of infection from the cervix and external genitalia to the trigonum undoubtedly occurs and the close relationship between erosion of the cervix and urethro-trigonitis is now generally accepted. Experimental work by Winsbury-Whitcomb and others supports this assumption, whilst clinically one finds it a waste of time to try and treat the chronic urethritis without, at the same time, attending to a cervical erosion, if present.

On the other hand, I believe that in the majority of cases the primary acute infection reaches the urethra as a direct ascending infection from the vulva. Whichever view is correct, the vulva and external genitalia are still the source of infection and I see no reason for blaming septic foci in nasal sinuses, gall-bladders, and other distant organs. The external urinary meatus is bathed in bacteria all day long, mostly non-pathogenic but contaminated with colon bacilli and other organisms after each act of defecation. Normally the healthy urethra is able to resist infection but unusual trauma such as prolonged unaccustomed cycling or defecation or coitus after a long interval, provide the minute abrasions and congestive state necessary for the organisms to gain entry to the tissues. As previously stated, the acute stage is not often seen in hospital but when it is, colon bacilli, streptococci or staphylococci can usually be cultured from the urethral smears. This is in contrast with the chronic form of this disease where urethral smears are either sterile or merely show diplococci, very occasionally staphylococci.

lococci, but hardly ever colon bacilli. Pus cells, however, are present if micturition has not occurred for several hours.

Six women with honeymoon urethro-trigonitis were encountered in the acute stage, but will be discussed later with the pyelitis cases.

Pyelonephritis.—I now wish to discuss the aetiology of pyelonephritis in women of this same age-group. The bulk of the literature on this subject is concerned with the possible route by which infection reaches the kidneys. The popular theory is that of hæmatogenous infection from some distant focus, that is, a bacteraemia. The second theory is that of ascending infection either up the lumen of the ureter, probably very rare, or via the peri-ureteric areolar tissue or the lymphatics. Final proof is still a long way off. The hæmatogenous theory supposes that organisms from the gall-bladder, appendix, colon, or hæmorrhoids, &c., somehow gain entry to the blood-stream setting up a bacteraemia which in turn causes a pyelonephritis. Obviously, this sequence of events can occur, but it seems most unlikely that it is the usual mode of kidney infection. There is no proof that a bacteraemia is present before the onset of a pyelitis, although admittedly, positive blood cultures have been recorded during the height of a rigor in pyelitis, but this does not prove that the infection is brought by the blood-stream to the kidney. In none of my cases was a rigor the presenting symptom, in fact the rigors, which were common before the use of sulpha drugs, generally occurred at the height of the infection, often only after several days, and this is surely more in favour of a theory that the rigor is due to a liberation of organisms from the kidney into the blood-stream and not vice versa.

Even assuming that a coliform or other bacteraemia does occur on occasion and remain symptomless—and this is non-proven—it must next be decided whether this bacteraemia can produce a clinical and pathological picture similar to the usual clinical pyelitis. Experimental pyelonephritis has been produced by many workers, notably Mallory (1940), and his colleagues, who injected saline emulsions of *B. coli communis* intravenously to rabbits. It was found that if the ureter had been previously obstructed, pyelonephritis developed in this kidney but not in its fellow. These results were obtained in 75% of their experiments. If the ureter was not interfered with no pyelonephritis developed in any of their animals. Lucas (1908) explained these results following ureteric obstruction by demonstrating a slowing of the venous circulation as a result of the raised intra-ureteric pressure, and he thought this allowed more time for the circulating organisms to gain a foothold. Although this theory could be used to explain the mode of infection in congenital hydronephroses, &c., it seems rather strong evidence against a hæmatogenous infection in an anatomically normal kidney. It might even be thought to explain the mode of infection in pyelitis of pregnancy were it not for the fact that we now know there is a greatly increased blood supply to the kidney during pregnancy; also, of course, the intra-ureteric pressure in pregnancy is less, not greater than normal (Traut, 1936). The supporters of the hæmatogenous theory believe that the coliform organisms come from the bowel, and I have heard it said, and it is stated in many textbooks, that some acute gastro-intestinal upset frequently precedes the onset of a pyelitis; this is *not* true. Admittedly, one case in the 246 suffered from diarrhoea lasting three days before her pyelitis, but in general the incidence of associated chronic gastro-intestinal disease was very low: 2 cases of mild cholecystitis, 2 probable peptic ulcers and a case of colitis: statistically insignificant in women of this age-group. Personally, I think that all the experimental evidence brought forward in favour of a blood-borne infection in pyelitis is most unconvincing, while much of it could be used as counter-evidence. The hæmatogenous infection seldom fits into the clinical picture whilst it is difficult to see how it can explain recurrent attacks of pyelitis.

The next theory is that of an ascending infection from the lower urinary tract—at one time the popular theory. Earlier workers assumed that the organisms travelled up the lumen of the ureter, but this is now thought to occur very rarely in the presence of a normal uretero-vesical orifice.

Ascending infection up the peri-ureteric areolar tissue remains for consideration; this is denied by many workers who assert that the lymphatics of the ureter run horizontally to the lumbar nodes and not vertically upwards; but some years ago Winsbury-White (1933b) demonstrated that Indian ink particles injected to the base of the bladder were eventually found in the hilum of the kidney. This work has not received the full recognition it deserves, especially in this country. Severe cases of urethro-trigonitis frequently have symptoms and signs of a peri-ureteritis and this I think is only a stage on the way to a clinical pyelitis.

evidence and the papers of many workers support this assumption, I have heard it argued that since these urethral findings are so common they can be of no significance. This is obviously a very important point and it was therefore decided to examine the urethra of a control series of women of the same age-group who had never at any time complained of any symptoms of abnormal micturition. The selection was rigid in that micturition by day must not be oftener than three-hourly, no nocturia, dysuria, scalding, urgency or stress incontinence was allowable, and there had to be no previous attacks of cystitis or pyelitis during childhood or pregnancy, or particularly following marriage. The results of this investigation are interesting. Before a series of 70 women with no abnormal symptoms could be collected, over 200 women had to be questioned closely; i.e. 2 in every 3 women gave a history of some previous disturbance of micturition. In the average parous woman, nocturia would appear to be the rule, while urgency and day frequency at hourly intervals are not unusual. This shows the high incidence of minor degrees of urogenital pathology and is surely a reflection on our profession for taking so little interest in it. The 70 symptomless, normal women were admitted to hospital for various conditions such as interval appendicectomy, herniotomy, incomplete abortions, minor orthopaedic lesions, &c., and they were all urethroscoped under general anaesthesia; the urines in every case were normal. A further 19 random controls were selected for urethroscopy who, although they were not suffering from any urinary symptoms at the time, did give a history of previous attacks of cysto-urethritis.

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Urethral polypi and hillocks were present in 5 of the 70 controls, but all of these 5 women were cases of abortions or salpingitis. Nothing pathological was found in 42 women suffering from non-genital lesions. Of the 19 women symptomless at the time, but having a previous urinary history, 13 or 68% showed evidence of urethral pathology. 70% of these 89 women were married and the only single woman to show any urethral changes was recovering from a salpingitis.

These figures do at least suggest that urethral polypi and hillocks are rare in a previously uninfected urethra, and that when present they do probably indicate an inflammatory condition.

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pyelitis occurring in a pregnant woman but owing to the associated physiological dilatation and stasis the symptoms are more severe and the treatment is more difficult.

Returning to the groups A and C on Table I, congenital anomalies and hydronephrosis, it is generally agreed that patients with congenital anomalies are more prone to urinary infection than normal individuals. One can readily understand that a few pathogenic organisms which would not affect a normal kidney might produce a serious infection in a congenital lesion with stasis, but given this stasis the route by which infection reaches the kidney is still disputed. Mallory's experiments (1940) with obstructed ureters show that a *haematogenous* infection is certainly possible under such circumstances, but I do not feel that it is the usual route and I would like to describe some cases where an ascending infection was more than likely.

CASE I.—A woman of 22 was admitted following defloration, with an acute urethritis later becoming a typical pyelitis. The clinical picture resolved rapidly with chemotherapy, but the patient was seen again ten days later after her discharge from hospital, with a return of symptoms on resuming normal sexual relations. Her pyelogram revealed a congenital hydronephrosis, later proved to be due to an aberrant vessel. This is a very good example of a congenital lesion with quite obvious stasis remaining perfectly symptomless for 22 years until it becomes infected from a urethritis.

CASE II.—A girl of 22 set off with a companion to cycle to Oxford. She was an experienced cyclist and having reached High Wycombe she became so "saddle-sore" she abandoned the effort and returned home by train. On the train she had scalding micturition with some terminal haematuria. Her urethritis persisted for five days when she was sent to hospital as a typical acute appendicitis because of tenderness in the right iliac fossa. The real cause of her trouble was infection in a bilateral megalo-ureter. She had repeated attacks of pyelitis after this one and finally died from uraemia.

There is little doubt that infection came from below in both of these cases.

There were 14 cases of honeymoon pyelitis which will now be considered in conjunction with the six cases of honeymoon urethritis already referred to, since they provide a very important aetiological link between urethro-trigonitis and pyelitis. Defloration urethritis is a very common condition, but it is usually mild and transient so that medical aid is seldom sought. It is hardly mentioned in the textbooks. Defloration pyelitis, however, is a well-recognized entity in the textbooks, most of which avoid any mention of the route by which infection gains access to the kidney. In all of these 20 women a careful history showed that following the attempt or the act of coitus, dysuria and frequency were experienced within a few hours, but it was several days before the unfortunate ones developed their pyelitis. Undoubtedly the primary infection was in the urethra in every case.

CASE III.—A 21-year-old girl was admitted from a Service hospital with a subsiding pyelitis. Three months previously she had been married during a forty-eight hour leave, and had developed a severe acute urethritis with terminal haematuria which lasted for five days. Usual tests for gonorrhoea were negative and a week later she went on a fourteen days' honeymoon which resulted in a further attack of urethritis, followed at the end of the week by a severe left pyelitis necessitating her admission to a hospital with rigors, &c. After this she had persistent frequency and dysuria with exacerbations following coitus until finally she developed a bilateral pyelitis during which I saw her. Her excretion pyelogram showed a congenital right dilated upper calix and a left small but otherwise normal-looking pelvis. Inspection revealed a very markedly contracted and oedematous urethra rendering instrumentation impossible without preliminary dilatation under an anaesthetic. Urethroscopy later showed a typical urethro-trigonitis but no polypi. Cystoscopy, however, revealed two complete left ureters, not showing in the excretion pyelogram. She also had a small cervical erosion. Here is a girl with congenital renal anomalies which remained symptomless for 21 years until she developed the urethritis. There can be little doubt that her pyelitis was an ascending infection.

An interesting postscript to this case was the fact that after her urine had been rendered sterile for three weeks, and her erosion cured, her next act of coitus brought on an acute urethritis lasting for forty-eight hours. She was therefore given sulphathiazole tablets with instructions to take 4 grammes during the twenty-four hours preceding coitus; this regime proved completely effective.

CASE IV.—This illustrates the point that "honeymoon" pyelitis is not confined to brides. A 33 year-old woman with one child aged 3 was admitted to hospital with a mild pyelitis and a history of frequency and dysuria for some months.

Examination only revealed a chronic urethritis with polypi. She became symptomless after diathermy fulguration of these polypi. However, she was readmitted twice more at five-week intervals and this made me suspicious. Close questioning revealed that her husband came on Service leave every five weeks and her attacks followed intercourse. Subsequent attacks of pyelitis and/or dysuria were prevented by her taking sulphathiazole tablets four hours before her husband's return. Subsequent treatment of his and her non-specific urethritis has resulted in a cure for both partners but the wife still insists on her prophylactic sulphathiazole.

Returning to Table I again, Group J shows that 58.5% of the pyelitis cases had urethroscopic evidence of the presence of urethro-trigonitis while Group K indicates that at least 54% of them had this urethro-trigonitis before the onset of their pyelitis,

Peri-ureteritis.—This is a well-recognized entity in America, but is seldom described in this country. The symptoms are a dull, almost continuous pain in one or both iliac fossae and groins, interspersed with mild spasms of colic. The symptoms are variously made worse or better by the onset of menstruation and this can be accounted for by the fact that the ovary and the lower end of the ureter have an almost common nerve and blood supply.

In the fairly large proportion of women who are still unrelieved of their symptoms by appendicectomy and attention to cystic ovaries, the passage of a ureteric catheter may produce a dramatic cure. In many cases the mere dilatation of the urethra alone will relieve the ureteric pain.

I believe that this peri-ureteritis is a definite clinical entity, closely related to urethro-trigonitis. One finds repeatedly that while ureteric catheterization is relatively painless in normal women, those suffering from urethro-trigonitis will complain of deep iliac fossa pain the moment the catheter is introduced.

If excretion pyelograms are performed during the active stages of an acute urethro-trigonitis, or during an exacerbation, very poor visualization of the upper urinary tract is obtained. This is due to pelvic and ureteric irritability producing rapid emptying as shown by the early concentration of dye in the bladder. This is only a transitory phenomenon and normal visualization returns when the urethral symptoms are relieved.

Although many radiologists will not agree, I believe that evidence of peri-ureteritis is frequently seen in excretion pyelograms particularly in cases of chronic urethro-trigonitis. Ureteric kinking if it is constant and cannot be corrected by alterations in breathing or posture, is pathological and is due to peri-ureteric adhesions.

The extreme kinking seen during pregnancy will return to normal so long as the patient does not develop a severe pyelitis. After a severe infection these kinks are definitely permanent. Similar, but obviously not such marked, permanent kinks are seen in urethro-trigonitis patients, who have never had an actual pyelitis, so that there is as much evidence in favour of an ascending peri-ureteritis from the trigone, as there is in favour of a descending one from the kidney.

Occasionally the ureters and pelves are seen filled all the way down, either due to a mild atonia or to a mild spasm at the lower end. This condition will generally return to normal when the urethral pathology is attended to.

Clinical data.—Table I shows the data of the 246 pyelitis cases under review and a detailed study leaves me convinced that a pyelitis very rarely develops in a patient with

TABLE I.—246 PYELONEPHRITIS CASES

	134 Non-pregnant	112 pregnant	Total
A Congenital lesions	6%	6%	6.0%
B Calculi	5.3%	5.3%	5.3%
C Hydronephrosis	5.9%	4.4%	5.2%
D Tuberculosis	1.5%	0.8%	1.2%
E Gross U.G. pathology	18.7%	16.5%	18%
F Previous U.G. infection	35.8%	35.6%	35.7%
G Patients with previous infection and/or gross U.G. pathology	50.7%	52.6%	51.2%
H Deformation	14 cases — 10.4%	—	10.4%
I Clinical proof of urethro-trigonitis	62%	55%	58.5%
K Symptoms of a urethritis preceding loin pain	61.7%	33.3%	54%

A combination of some gross pathology, or a urethrotrigonitis or a previous history of urinary tract infection was present in 81% of the 246 women.

a previously anatomically normal or uninfected renal tract. It will be seen that 18% of the non-pregnant and 16% of the pregnant women had some gross urological pathology which in many cases called for major surgical intervention. The next important finding was that 35% of the non-pregnant and 35% of the pregnant women gave a history of some previous urinary tract infection, such as, a previous attack of pyelitis, cystitis, or a urethritis, severe enough to make them seek medical advice. Many more women complained of attacks of frequency, dysuria, urgency, or perhaps even terminal hæmaturia which they called a chill on the bladder, but did not bother to see a doctor about it. This means that preceding the attack of pyelitis under consideration there was proof of some urinary tract pathology in 50% of the non-pregnant and 52% of the pregnant women.

The incidence of pyelitis of pregnancy is very little greater than the incidence of pyelitis in non-pregnant women of the same age-group. The ætiological factors appear to be the same and there is nothing special about pyelitis of pregnancy; it is merely a

pyelitis occurring in a pregnant woman but owing to the associated physiological dilatation and stasis the symptoms are more severe and the treatment is more difficult.

Returning to the groups A and C on Table I, congenital anomalies and hydronephrosis, it is generally agreed that patients with congenital anomalies are more prone to urinary infection than normal individuals. One can readily understand that a few pathogenic organisms which would not affect a normal kidney might produce a serious infection in a congenital lesion with stasis, but given this stasis the route by which infection reaches the kidney is still disputed. Mallory's experiments (1940) with obstructed ureters show that a hæmatogenous infection is certainly possible under such circumstances, but I do not feel that it is the usual route and I would like to describe some cases where an ascending infection was more than likely.

CASE I.—A woman of 22 was admitted following defloration, with an acute urethritis later becoming a typical pyelitis. The clinical picture resolved rapidly with chemotherapy, but the patient was seen again ten days later after her discharge from hospital, with a return of symptoms on resuming normal sexual relations. Her pyelogram revealed a congenital hydronephrosis, later proved to be due to an aberrant vessel. This is a very good example of a congenital lesion with quite obvious stasis remaining perfectly symptomless for 22 years until it becomes infected from a urethritis.

CASE II.—A girl of 22 set off with a companion to cycle to Oxford. She was an inexperienced cyclist and having reached High Wycombe she became so "saddle-sore" she abandoned the effort and returned home by train. On the train she had scalding micturition with some terminal hæmaturia. Her urethritis persisted for five days when she was sent to hospital as a typical acute appendicitis because of tenderness in the right iliac fossa. The real cause of her trouble was infection in a bilateral megalo-ureter. She had repeated attacks of pyelitis after this one and finally died from uræmia.

There is little doubt that infection came from below in both of these cases.

There were 14 cases of honeymoon pyelitis which will now be considered in conjunction with the six cases of honeymoon urethritis already referred to, since they provide a very important ætiological link between urethro-trigonitis and pyelitis. Defloration urethritis is a very common condition, but it is usually mild and transient so that medical aid is seldom sought. It is hardly mentioned in the textbooks. Defloration pyelitis, however, is a well-recognized entity in the textbooks, most of which avoid any mention of the route by which infection gains access to the kidney. In all of these 20 women a careful history showed that following the attempt or the act of coitus, dysuria and frequency were experienced within a few hours, but it was several days before the unfortunate ones developed their pyelitis. Undoubtedly the primary infection was in the urethra in every case.

CASE III.—A 21-year-old girl was admitted from a Service hospital with a subsiding pyelitis. Three months previously she had been married during a forty-eight hour leave, and had developed a severe acute urethritis with terminal hæmaturia which lasted for five days. Usual tests for gonorrhœa were negative and a week later she went on a fourteen days' honeymoon which resulted in a further attack of urethritis, followed at the end of the week by a severe left pyelitis necessitating her admission to a hospital with rigors, &c. After this she had persistent frequency and dysuria with exacerbations following coitus until finally she developed a bilateral pyelitis during which I saw her. Her excretion pyelogram showed a congenital right dilated upper calix and a left small but otherwise normal-looking pelvis. Inspection revealed a very markedly contracted and œdematous urethra rendering instrumentation impossible without preliminary dilatation under an anæsthetic. Urethroscopy later showed a typical urethro-trigonitis but no polypi. Cystoscopy, however, revealed two complete left ureters, not showing in the excretion pyelogram. She also had a small cervical erosion. Here is a girl with congenital renal anomalies which remained symptomless for 21 years until she developed the urethritis. There can be little doubt that her pyelitis was an ascending infection.

An interesting postscript to this case was the fact that after her urine had been rendered sterile for three weeks, and her erosion cured, her next act of coitus brought on an acute urethritis lasting for forty-eight hours. She was therefore given sulphathiazole tablets with instructions to take 4 grammes during the twenty-four hours preceding coitus; this regime proved completely effective.

CASE IV.—This illustrates the point that "honeymoon" pyelitis is not confined to brides. A 33 year-old woman with one child aged 3 was admitted to hospital with a mild pyelitis and a history of frequency and dysuria for some months.

Examination only revealed a chronic urethritis with polypi. She became symptomless after diathermy fulguration of these polypi. However, she was readmitted twice more at five-week intervals and this made me suspicious. Close questioning revealed that her husband came on Service leave every five weeks and her attacks followed intercourse. Subsequent attacks of pyelitis and/or dysuria were prevented by her taking sulphathiazole twenty-four hours before her husband's return. Subsequent treatment of his and her non-specific urethritis has resulted in a cure for both partners but the wife still insists on her prophylactic sulphathiazole.

Returning to Table I again, Group J shows that 58.5% of the pyelitis cases had urethroscopic evidence of the presence of urethro-trigonitis while Group K indicates that at least 54% of them had this urethro-trigonitis before the onset of their pyelitis,

as judged by the fact that symptoms of urethritis preceded the pyelitis, often by several days.

Taking the whole series, a combination of some gross pathology, or urethro-trigonitis or a previous history of urinary tract infection was present in 81% of the 246 women.

I would suggest therefore that pyelitis is seldom a primary disease in itself but is merely a dramatic incident occurring during the course of a generalized urinary tract infection.

In conclusion I would say that the female urethra is a very common source of latent urinary tract infection, neglect of which leads much needless suffering.

As for the relationship of the urethra to pyelonephritis, although actual proof is lacking the theory of ascending infection has as much, if not more, clinical evidence in its favour than any other theory.

There appears little doubt that a great majority of pyelonephritis patients have an underlying pathological condition and for this reason I would make a plea for their being regarded as surgical, not medical, cases, since only by this means will they receive full urological investigation.

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Mr. H. P. Winsbury-White: A valuable experimental study bearing on the relationship between urethral and renal infections has been carried out by Helmholtz of the Mayo Clinic. He injected cultures of living organisms into the urethra and on killing the animals (rabbits) the organisms were identified in inflammatory lesions in the renal substance. A point of considerable practical interest arising from these experiments is that in several instances urine taken from the renal pelvis at the time the kidneys were removed failed to reveal the presence of organisms on careful laboratory investigation.

The phenomenon of renal infection which is not substantiated by urinary findings is well known to us all in certain cases of renal abscess, but the co-existence of the two states in mild degrees of renal infection is not so well known. This is largely because in these mild infections we are almost entirely dependent on animal experiment for confirmation of the presence of a renal lesion.

Helmholtz's experiments, however, open up a line of inquiry we can profitably follow in early cases of kidney pain, for if we investigate the urethra in all such cases, and in some of them find a lesion, and the treatment of this alleviates the renal symptom, it is not an unreasonable conclusion that there is a renal change which owes its origin to the urethral lesion.

Let us take a commonplace example: A young woman has had intermittent pain in one loin on and off for several years. There is mild chronic frequency which with the renal pain tends to flare up from time to time. Neither the laboratory report on the urine, nor the intravenous urograms throw any light on the cause of the symptoms. The cystoscopic picture shows that the general bladder cavity is quite normal in appearance, and unless we examine the front of the trigone and the internal urinary meatus with great care, it may escape our notice that inflammation exists in one or both of these localities. The examination of such a case should not be terminated without urethroscopy. Commonly this procedure will show chronic inflammatory changes in the posterior urethra.

The whole area of inflammation just referred to is small but compact, it can be properly described as a urethrotigonitis, or in some cases a urethro-cervico-trigonitis, because the internal urinary meatus is also involved.

The lymphatic connexion between this bladder-neck region and the kidneys is of course outside the bladder and ureters, and the healthy-looking vesical mucosa which is seen on cystoscopy is apt to distract one's attention from the probability that the urethro-trigonitis has anything to do with the renal symptoms, but the disappearance—if this occurs—of the renal pain as a result of the appropriate treatment of the urethro-trigonitis is proof enough of the interdependence of the two widely separated conditions.

Developmentally the posterior urethra arises as a protrusion from the bladder. The zone comprising the front of the trigone, the internal urinary meatus and the posterior urethra is indeed entitled to our earnest attention because it is also involved in the following well-known conditions: Median bar formation; fibrous constriction of the internal urinary meatus; and the various prostatic changes we know so well.

Is it likely that these commonplace states at the bladder-neck suddenly begin to develop without apparent reason; or are they preceded by gradually occurring and insidious changes in the region concerned? Such a question must lack a definite answer unless routine observations are made in young patients who develop disturbances of micturition.

I have always approached the examination of children and young adults with chronic frequency and other disturbances of micturition, with the feeling that one is probably dealing with the incipient stages of diseased states with which we are all familiar in adult life.

In looking back over one's own cases of urethro-trigonitis which have been associated with upper urinary tract symptoms, one can divide them into several categories according to the nature of the renal symptoms: (1) Intermittent aching in the loin; (2) chronic aching in the loin; (3) attacks of pyelitis; (4) chronic pyelonephritis. There is a background of frequency of micturition in all these cases.

The proof of the dependence of the upper urinary tract changes and symptoms on the lower urinary tract pathology lies in the improvement in the renal symptoms, which goes hand in hand with the improvement in the urethro-trigonitis as the latter is given the appropriate treatment.

I have found it quite usual to control the tendency to attacks of pyelitis, by treating an existing urethro-trigonitis. I could recite innumerable cases of other kinds where kidney symptoms have been controlled in the same way.

One particular group of cases should be mentioned, however, because it is apt to be very distressing. I refer to attacks of cystitis and pyelitis which follow quickly upon sexual intercourse. Such a train of events is dependent upon trauma to a granulosomatous urethra, and the symptoms come on within forty-eight hours of intercourse. I recently had a patient who complained of five attacks of cystitis two of which were accompanied by pyelitis. She was quite definite that each attack followed within forty-eight hours of intercourse. Naturally both she and her husband were worried about these incidents. Urethroscopy showed several large polypi in the posterior urethra. After appropriate treatment of the urethra, the attacks ceased.

Organisms in the urine.—It has been of some interest to divide these cases with renal symptoms into categories in relation to the presence of organisms in the urine, and in an ascending order of severity: (1) No organisms at all; (2) organisms intermittently in the bladder urine; (3) organisms chronically in the bladder urine; (4) organisms intermittently in the kidney urine; (5) organisms chronically in the kidney urine.

Modern anatomists have demonstrated lymphatics between rectum, cervix and bladder-neck. We know how *B. coli* is attracted to a well-prepared soil.

The lymphoid collections in the submucous tissue of the posterior urethra and bladder-neck which have been demonstrated by different research workers seem to be the initial foci of infection in these parts.

TREATMENT

Treatment which I have carried out for many years on the urethral foci is by urethral dilatation, but fulguration of urethral polypi is essential in certain cases. I believe that the benefit from the urethral dilatation is by promoting drainage from foci of infection.

There are, however, so many different ways in which this treatment can be carried out that we may expect an equal variety of results. It is therefore very unsatisfactory to state that urethral dilatation is good or it is bad, without giving details as to how the treatment has been done.

There are three phases in the symptoms following urethral dilatation. Each one of these phases varies in different cases, according to the circumstances of the case, and the judgment shown by the operator.

(1) *The immediate reaction.*—Often the only symptom is dysuria, lasting a few hours; but cystitis may occur. This generally means that the dilatation has been carried too far. I believe that it takes about two weeks for all local signs of an instrumentation to pass, therefore I never give the second dilatation until three weeks have elapsed since the first one.

(2) *The period of improvement of the symptoms under treatment.*—This is extremely variable, it generally lasts for about three weeks after the first treatment, but it may last for only three days, or it may persist for many months. In some cases no improvement need be expected in renal symptoms. If no improvement results in bladder symptoms in spite of several treatments, the genital system should be searched carefully, to be sure that there is not some adjacent focus of infection which has been overlooked.

(3) *The tendency to relapse.*—The first sign of this is the signal for the treatment to be repeated.

Technique

There are many faults which can be committed in connexion with this treatment, and in the course of having treated many hundreds of women, I have been guilty of many of them. Perhaps the easiest mistake to make is to carry the dilatation too far at a particular treatment. The next common mistake is to give the treatment too often.

Instruments

In women straight metal sounds graduated in the Charrière scale are the best. On the occasion of the first visit the calibre of the urethra should be gauged by taking a 24 Ch. instrument. On this occasion further dilatation should proceed only until an instrument is gently gripped. Subsequent dilations should proceed so as to increase one Charrière at each visit. For most women a maximum of 30 Charrière should be regarded as the top size, but many should never reach this; in odd cases 32 Charrière is the correct maximum size. One can only condemn the use of Hagar's cervical dilators; they are too crudely graduated for this purpose.

Intervals between the dilations.—For adults these should as a rule be gradually extended, although it may be necessary to vary these at certain points, according to progress. The intervals I generally allow after the first interval of three weeks are expressed in months as follows: 1, 1½, 2, 3, 4, 6, 9, 12, but it is important to be ready to extend an interval between treatment, when there is no tendency for symptoms to return.

It should be hardly necessary to add that badly conducted instrumentation will do more harm than good.

Mr. Clifford Morson drew attention to the experiments of Mottram on the effect of irradiation of the large bowel in which he showed that, when the mucin-forming cells of the mucous membrane were damaged, the colon bacilli migrated from its surface to the pericolic lymphatics and thence to the blood-stream. One could therefore postulate that a long-standing chronic constipation or other chronic lesion of the large gut which interfered with the function of the goblet cell would cause an infection of the urinary tract with the *Bacillus coli*. The bowel cannot be ruled out entirely as a source of infection. There were unquestionable cases of colon bacilluria in the female associated with lesions of the bowel such as diverticulitis and chronic constipation.

Mr. J. Gabe: I have had numerous opportunities of observing the urethroscopic and cystoscopic appearances described by Mr. Hanley and can testify to the favourable response of patients to appropriate measures, e.g. urethral dilatation, fulguration of polyp and cauterization of cervix. I noticed that neither Mr. Hanley nor Mr. Winsbury-White mentioned the frequent finding of residual urine in these cases.

I have often met with chronic urethrotigonitis in cases of pyelitis of pregnancy. To quote merely one example. A young woman had an attack of "cystitis" four months after marriage. Shortly after this she became pregnant. In the puerperium she had an attack of left-sided pyelitis but pain persisted in the left loin after the acute attack had subsided. Examination revealed the coexistence of a large cervical erosion, urethrotigonitis and a large left-sided hydronephrosis. Within a few months she again became pregnant and the left kidney was removed to prevent further trouble. The concomitant lesions are in the process of being treated.

One has heard it said that abnormal appearances such as have been so well and so fully described by Mr. Hanley are due to instrumental trauma, but having seen many normal urethrae one knows this is not true.

I might add that when I first became interested in this subject as the result of seeing Mr. Winsbury-White's work at St. Paul's Hospital I felt rather sceptical, but I must confess myself completely in agreement with the findings and with the efficacy of the established methods of treatment.

[April 25, 1946]

The following Cases and Specimens were shown:

Kidney

- (1) Crossed Renal Ectopia with Cystine Calculus in the Ectopic Kidney (Radiographs);
- (2) Calcium Infarction of the Kidneys (Radiographs).—Mr. J. D. FERCUSSON.

- (1) Partial Nephrectomy for Caliceal Calculi; (2) Completely Calcified Kidney (Radiographs).—Mr. J. GABE.

Solitary Cyst Simulating Splenomegaly.—Mr. HOWARD HANLEY.

Late result of von Lichtenberg's Operation.—Mr. MAURICE LEE.

Congenital Bladder Neck Obstruction with Crossed Renal Ectopia.—Mr. H. K. VERNON.

Ureter

Kidney and Radiographs of Gunshot Wound of Ureter.—Mr. A. W. BADENOCH.

Denervation of the Ureter for Persistent Pain (Patient was Demonstrated).—Mr. H. G. HANLEY.

Massive Ureteric Calculi.—Mr. H. K. VERNON.

Bladder

Leiomyosarcoma of Urinary Bladder.—Mr. J. GABE.

Cysto-Prostatectomy for Enlarged Villous Growth of Bladder.—Mr. MAURICE LEE.

External Genitals

Congenital Venous Angioma of Scrotum in a Boy of 4 Years. For Confirmation of Diagnosis and Opinion Re Treatment.—Mr. E. W. AINSWORTH-DAVIS.

(1) Seminoma; (2) Hæmatocele of Epididymal Cyst.—Mr. E. W. RICHES.

[June 27, 1946]

Urological Reflections

By SIR HENRY WADE, C.M.G., F.R.C.S.Ed.

AFTER some introductory remarks on the methods of urological diagnosis in vogue when he was a student, Sir Henry Wade continued:

Determination of renal function.—The determination of renal function by the physician is most commonly made by carrying out a urea concentration test or a similar method. In my experience the simpler method of blood examination, wherein the blood urea is estimated, the urea nitrogen or non-protein nitrogen and creatinine determined, has proved a most valuable diagnostic aid. There is, however, one method that I would put first of all, which many of the younger urologists are liable to overlook, and that is, the examination of the patient's tongue.

The Operative Treatment of Prostatic Disease: The prostatic gamble.—Castration: The first form of treatment I saw carried out for the relief of prostatic obstruction due to simple prostatic hypertrophy was by castration, a barbarous procedure, but one based upon an idea which has in it a certain germ of great truth.

Vasectomy: As the unfortunate patients occasionally suffered from a complete mental upset following this treatment it was modified to that of vasectomy, which also did no good but fortunately did no appreciable harm.

I left my post as a young Resident in the Royal Infirmary of Edinburgh to proceed to South Africa in the capacity of a civil surgeon, an individual who was described as one who received the pay of a Major, the rank of a Captain and the dress of a Hindu dispenser, and there was attached to the No. 1 General Hospital at Wynberg where my colleagues were Sir Charles Gordon-Watson, Frank Gairdner and certain others. After a stay of three weeks we were sent up country and for a year and ten months I never slept under a roof and lived on the open veldt and ultimately returned to teach Anatomy under Sir William Turner in the dissecting room of Edinburgh University during the winter, a contrast in existence that it took all my will power to survive. Following this came my further training in surgery as Resident and Clinical Tutor and Private Assistant, and I had the good luck to be appointed Conservator of the Royal College of Surgeons' Museum. I now decided on a course that at the time was thought to be unusual if not dangerous, to give up the practice of surgery entirely and become a whole-time Pathologist to the Royal Infirmary, Edinburgh, for two years. All the post-mortem examinations done on surgical cases were carried out by myself, and in certain of these the operation of prostatectomy had been carried out and I was interested to observe how frequently there was revealed a pronounced degree of hydronephrosis and how sometimes the renal secreting tissue was reduced to a thin membrane covering bags of water.

Visit to St. Peter's Hospital.—These were the days when Freyer was at the height of his well-deserved fame, and I came South to see him operate at St. Peter's and I well remember a case he dealt with. In company with a few others I sat on a bench in the operating theatre: facing us was the operating table and beyond it the wash-hand basin opposite which a clean roller towel hung up. The operation was carried out speedily and simply by that most dexterous surgeon, who removed the gland in one piece, introduced his drainage tube and enfolded the skin around it by suture and brought the specimen over to where we were sitting and demonstrated to us to his satisfaction the fact that he had removed the entire gland. Now at this stage a controversy existed as to whether his statement was in truth correct. Thomson Walker supported his view, and in common with others I studied the question.

The method I employed was first of all to make whole sections of 50 specimens that had been recently presented to the College Museum as illustrating simple prostatic hypertrophy. An interesting result followed this study where I found that 10% of these, unknown to the operator, were the site of a certain variety of carcinoma, which as we now know develops not infrequently from the simple enlargement. I also had whole sections made of the prostatic beds obtained at the post-mortem examination and these showed that the condition of simple hypertrophy was a hyperplasia limited in its extent which formed a rind or false capsule from the compressed and condensed uninvolved prostatic tissue, from beneath which the area of hypertrophy was enucleated most frequently in a single mass. Freyer, who had done so very much for humanity, was unconvinced. This would have mattered little if the consequences had not been serious, for, if simple hypertrophy is present and the rind or false capsule is formed the circumstances are ideal for the treatment of the case by suprapubic enucleation; on the other hand prostatism may arise from other causes especially fibrosis or interstitial prostatitis and prostatic carcinoma; in neither of these is a false capsule formed and an attempt at enucleation from above may be fraught with serious consequences where the line of cleavage is extra-capsular involving the prostatic veins and lymphatics and the cellular tissue planes of the pelvis.

At this period the mortality that attended the operative treatment for prostatectomy was extremely high—in one Institution with which I was associated for ten years down to 1913 it amounted to 25% and on returning again to duty after being absent for five years' service in 1920 it still stood at 25% and during the year 1916 it had amounted to 40%.

Hugh Hampton Young.—The results of the work I carried out were shown by me at the International Medical Congress held in London in 1913, and there I first met Hugh Hampton Young of Baltimore and John Cunningham of Boston. The former was keenly interested in my exhibit which he published in the *Annals of Surgery* with unlimited illustrations in black and white and in colour. I was also invited to attend the following year at Johns Hopkins Hospital when the Buchanan Brady Institution founded by Diamond Jim Brady was to be opened as a Urological Department. The advent of war prevented this, but in 1920 the invitation was again extended and for several months I was in America and most of the time with Young in Baltimore. I arrived on a Sunday as his senior assistant was trying to get through to Atlantic City to ask his Chief's advice as regards a case that he had operated on in which he had used his punch to remove the bladder neck for interstitial prostatitis. By those who have been his assistants the value of this method was fully appreciated, but the handicap of the associated hæmorrhage was also realized so that his assistant Caulk, who was now in St. Louis, modified the punch by using a diathermy knife to divide the bladder neck, and another of his colleagues, Gerratty, introduced the sphincterotome which cuts through the bladder neck.

The practice of transurethral prostatectomy now swept through the United States and many modifications of the original method were introduced. Most of these were modified forms of the diathermy knife. Bumpus in the Mayo Clinic at Rochester applied the diathermy current to the gland to be removed before it was cut, but this was modified later by Thomson who used what really was, in principle, the original Young's punch and subsequently arrested the bleeding by diathermy.

Perineal prostatectomy: Like certain others I at this time took unkindly to a prostatic gamble. I was drawn to the technique of perineal prostatectomy practised by Hugh Young, a procedure he adopted in all his cases of simple enlargement. To carry it out required a special technique with special instruments, a very accurate anatomical knowledge and well-trained team. As one who practised general surgery, the lessons I learned when doing this operation improved my operating technique in certain other cases.

Malignant disease.—It was essentially similar to that adopted in the operation of total excision of the prostate by the perineal route for malignant disease. A knowledge of it enabled the treatment of malignant disease of the prostate by interstitial radiation to be properly carried out. It also improved my technique in the operative treatment of carcinoma of the rectum by excision, particularly where simple prostatic enlargement was combined with carcinoma of the rectum, a not-infrequent combination.

Total excision of the genital tract for tuberculous disease.—A technique very similar was employed by Young in his operation of total excision of the genital tract for tuberculous disease. The epididymis, vas deferens, seminal vesicles and frequently a part of the prostate were removed in one piece, the exposure being similar to that for

perineal prostatectomy. The urethra, however, was not opened and the prostate and vesicles were brought down by Young's seminal vesical tractor. In my opinion this operation necessitates the most delicate and most skilful operative dexterity in the practice of urology.

Congenital vesical sphincteric stenosis (prostatic valve).—When I was Conservator of the Royal College of Surgeons' Museum, it was my custom every Tuesday at two in the afternoon to lecture to senior students and graduates on various aspects of surgical pathology, and when dealing with cases of neuromuscular inco-ordination or achalasia, I used to demonstrate specimens of what John Thomson, the father of all paediatric physicians, called congenital vesical sphincteric stenosis, a condition found sometimes in the stillborn, met with in infants and not uncommonly seen in later life, and one which, by the backward pressure it exercises, may prove fatal by the damage it causes to renal functional activity. As far as I am aware Hugh Young was the first to treat this condition by operation. In 1920 I saw him operate on one of his first cases, a youth called Bobby. The bladder had previously been opened and on viewing its interior, the widely-opened internal sphincter and the dilated prostatic urethra could be inspected. Young employed a specially made tiny punch to remove what he described as the prostatic valve causing the obstruction. In all his subsequent cases Young described the condition as one of congenital prostatic valve.

Stricture of the ureter.—During this visit I was introduced by Guy Hunner to a new disease, which he described as stricture of the ureter, and saw him carry out the treatment which he did by making a bulbous end of wax on the tip of a ureteral catheter and 15 cm. from the tip he made a spindle of molten wax as a dilator. A Kelly cystoscope combined with the air inflation with the patient in the genu-pectoral position was employed. Despite the charm of the surgeon I did not fall for his operation, but that is another story.

The treatment of bladder tumours by diathermy.—When Beer of New York was a student at Vienna he saw Nitze removing bladder tumours by trans-urethral snares. He suggested the employment of diathermy but received no encouragement. On his return to New York, however, he conducted his research and Wappler Brothers made for him the necessary instruments and thus was introduced a line of treatment which has revolutionized the practice of urology in one direction and proved of great benefit in cases of villous papilloma of the bladder and certain other conditions.

The role of surgery in renal tuberculosis.—It has been my lot to excise many kidneys, the site of tuberculous disease. At the same time, in almost all cases, this has been accompanied by an explanation and an apology to my audience and a hope for a better treatment in the future. The explanation of my conduct is that as a student and House Surgeon there was hardly an operating day passed but in several of the seven operating theatres of my hospital joints were excised or bones resected for tuberculous disease. This treatment is now unknown, for at the same time there was in Liverpool Thomas and his nephew, Robert Jones, showing how a better result could be obtained, without mutilation, by conservative means. Their influence gradually prevailed, so that such operations as I have mentioned are now unknown. If such be the case, why is a similar result not possible in renal surgery? Why cannot a cure by conservative measures be also accomplished here? The underlying process of natural healing is identical in both cases. The explanation, of course, is in the environment of the disease. In both the infection is combated and walled off and the debris conveyed to a free surface and there discharged and the sinus healed. Unfortunately the free surface in the kidney is the renal pelvis and into it the debris containing the tubercle bacilli is discharged to reinfect the kidney at some other part and to infect the ureter and bladder. By this means the process of cure and re-infection continues, until the organ is ultimately destroyed and a so-called auto-nephrectomy results. In the meantime a systolic bladder has been produced which, despite excision of the organ, may persist and by its backward pressure ultimately destroy the renal functioning tissue of the remaining kidney and lead to death by uræmia. I have had several such cases and have tried various remedies, the most successful of which was the transplantation of the remaining ureter into the pelvic colon. It is my fervid hope that the day is not far distant when nephrectomy for renal tuberculosis will be required no longer. As it is to-day, however, if it is indicated, the surgeon operating is under an honourable obligation to care for his patient for two years afterwards, to arrange post-operative sanatorium treatment, and in certain cases to advocate pre-operative sanatorium preparatory treatment.

Transplantation of the ureters into the pelvic colon and the establishment of a cloaca.—This operative procedure that is associated especially with Stiles, Grey Turner, Coffey and Charles Mayo is now well established and is indicated in certain conditions. It is

The method I employed was first of all to make whole sections of 50 specimens that had been recently presented to the College Museum as illustrating simple prostatic hypertrophy. An interesting result followed this study where I found that 10% of these, unknown to the operator, were the site of a certain variety of carcinoma, which as we now know develops not infrequently from the simple enlargement. I also had whole sections made of the prostatic beds obtained at the post-mortem examination and these showed that the condition of simple hypertrophy was a hyperplasia limited in its extent which formed a ring or false capsule from the compressed and condensed uninvolved prostatic tissue, from beneath which the area of hypertrophy was enucleated most frequently in a single mass. Freyer, who had done so very much for humanity, was unconvinced. This would have mattered little if the consequences had not been serious, for, if simple hypertrophy is present and the ring or false capsule is formed the circumstances are ideal for the treatment of the case by suprapubic enucleation; on the other hand prostatism may arise from other causes especially fibrosis or interstitial prostatitis and prostatic carcinoma; in neither of these is a false capsule formed and an attempt at enucleation from above may be fraught with serious consequences where the line of cleavage is extra-capsular involving the prostatic veins and lymphatics and the cellular tissue planes of the pelvis.

At this period the mortality that attended the operative treatment for prostatectomy was extremely high—in one Institution with which I was associated for ten years down to 1913 it amounted to 25%, and on returning again to duty after being absent for five years' service in 1920 it still stood at 25% and during the year 1916 it had amounted to 40%.

Hugh Hampton Young.—The results of the work I carried out were shown by me at the International Medical Congress held in London in 1913, and there I first met Hugh Hampton Young of Baltimore and John Cunningham of Boston. The former was keenly interested in my exhibit which he published in the *Annals of Surgery* with unlimited illustrations in black and white and in colour. I was also invited to attend the following year at Johns Hopkins Hospital when the Buchanan Brady Institution founded by Diamond Jim Brady was to be opened as a Urological Department. The advent of war prevented this, but in 1920 the invitation was again extended and for several months I was in America and most of the time with Young in Baltimore. I arrived on a Sunday as his senior assistant was trying to get through to Atlantic City to ask his Chief's advice as regards a case that he had operated on in which he had used his punch to remove the bladder neck for interstitial prostatitis. By those who have been his assistants the value of this method was fully appreciated, but the handicap of the associated hæmorrhage was also realized so that his assistant Caulk, who was now in St. Louis, modified the punch by using a diathermy knife to divide the bladder neck, and another of his colleagues, Gerratty, introduced the sphincterotome which cuts through the bladder neck.

The practice of transurethral prostatectomy now swept through the United States and many modifications of the original method were introduced. Most of these were modified forms of the diathermy knife. Bumpus in the Mayo Clinic at Rochester applied the diathermy current to the gland to be removed before it was cut, but this was modified later by Thomson who used what really was, in principle, the original Young's punch and subsequently arrested the bleeding by diathermy.

Perineal prostatectomy: Like certain others I at this time took unkindly to a prostatic gamble. I was drawn to the technique of perineal prostatectomy practised by Hugh Young, a procedure he adopted in all his cases of simple enlargement. To carry it out required a special technique with special instruments, a very accurate anatomical knowledge and well-trained team. As one who practised general surgery, the lessons I learned when doing this operation improved my operating technique in certain other cases.

Malignant disease.—It was essentially similar to that adopted in the operation of total excision of the prostate by the perineal route for malignant disease. A knowledge of it enabled the treatment of malignant disease of the prostate by interstitial radiation to be properly carried out. It also improved my technique in the operative treatment of carcinoma of the rectum by excision, particularly where simple prostatic enlargement was combined with carcinoma of the rectum, a not-infrequent combination.

Total excision of the genital tract for tuberculous disease.—A technique very similar was employed by Young in his operation of total excision of the genital tract for tuberculous disease. The epididymis, vas deferens, seminal vesicles and frequently a part of the prostate were removed in one piece, the exposure being similar to that for

Section of Experimental Medicine and Therapeutics

President—E. N. ALLOTT, F.R.C.P.

[May 14, 1946]

DISCUSSION ON THE LIFE AND DEATH OF THE RED BLOOD CORPUSCLE -

Dr. Sheila T. Callender: Our recent work on the life of the red cell has been concerned with an attempt to establish a norm for the Ashby technique by the process of bleeding and immediate transfusion of healthy volunteers. Our subjects were 6 male medical students and 4 women working in our department. They all belonged to Group A or B and were Rh positive. Details of our procedure have been described elsewhere (Callender, Powell and Witts, 1945). Two of the men have been excluded from our final results. One because he developed a small pleural effusion, presumably tuberculous, and the other because he had a transfusion reaction due to the use of a "dangerous universal donor".

In discussing our results I will deal first with the findings in men, for in the women there is the complicating factor of menstruation. In all four normal men the findings are essentially similar. An average of four counts made by two observers was taken each time, and the non-agglutinable counts were plotted against time from transfusion. The graphs fitted are practically linear, except for a short period at the beginning and end. At the beginning there is considerable irregularity of the counts and a tendency for an initial period of more rapid destruction. At the end of the graphs there is a tailing out. According to our results, however, it is not great and for practical purposes can be disregarded. We have found consistently that the average life of the transfused red cells is about sixty days and that the rate of destruction is 0.83% of the initial amount per day.

The period of initial more rapid destruction has been noted in hypochromic anæmias previously studied where the red cell count has been raised above normal, and in those normal men in whom the amount of blood given was rather more than that removed. This is of interest in relation to recent American work (Pace, Consolazio and Lozner, 1945) on transfusion as a method of producing tolerance to hypoxia in high altitude flying, and it may be one of the reasons why the observed beneficial effects were relatively short lived.

adopted in all cases of extroversion of the bladder, partial or complete. In the year 1908 Sir Harold Stiles operated on a young patient, now Mrs. X, who has her home in Fife, and is alive and in excellent health to-day. In my experience the next most important indication is the presence of an extensive vesico-vaginal fistula incapable of plastic repair, or associated with complete destruction of the vesical sphincter. The success of the operation in these cases and the relief that is produced are most impressive. On the other hand, although I have operated on many cases for malignant disease, the results have been very far from satisfactory, and I have come to the conclusion that, in these cases, there is a factor perhaps physical, perhaps psychical that tells against the success of the operation.

Reflections on the future of urology.—I regret that I must conclude with some sombre reflections. My fear for you arises from the tools you have fashioned, the skill you have shown and the dexterity you possess. Others may seek your aid, asking for your services as a technician, and not as a physician. Be warned against this insidious evil. Never examine an organ or a region, only examine a patient. Remember that medicine is an art, not a science, and that you possess many an instrument to tell you when a man is ill, but none to tell you when he is well. Man is not a motor car and susceptible to similar methods of overhaul and repair. Psychological derangements, particularly in the young female, may simulate actual organic disease. It is important to bear in mind that the final conclusions you came to when you stated a fact were not a diagnosis but a confirmed observation of the presence of an abnormality in the organ you have examined and from the limited vision of the specialist you may sincerely and honestly believe it to be the cause of ill-health; while in truth this is due to a factor outwith your knowledge. At first it would appear that the answer to this is the establishment of the Clinic or Poly-Clinic or the Health Centre, the creation of an Institution where a whole-time Staff would be available to carry out a complete investigation with all the aids known to medicine and in all the departments of medicine. In any modern rationalized surgical service the value of such an organization surely is self-evident, but is it the final answer? The premise we lay down is that the majority of ailments of which mankind complain are incapable of exact scientific demonstration. "Diagnosis", said a famous doctor, "is 50% guess work. Some guess better than others. Doctoring means sureness of personal judgment as well as brilliance in clinical assessment." To be a great urologist you must also be a great doctor and practise the art of surgery as it is seen at its best in certain fine old-fashioned general practitioners. I recall one summer morning meeting in his consulting room in the Peter Bent Brigham Hospital of the Harvard University in Boston that great surgeon, Dr. Harvey Cushing, the father of neuro-surgery; with a naughty twinkle in his eye he told me that he had just seen a case sent to him as one of pituitary tumour and it really was a case of an over-worked stenographer who required six weeks' holiday.

Health Centre.—The Health Centre may prove to be an Institution of the very greatest value. On the other hand a so-called Diagnostic Clinic may have quite a contrary effect, for it never should be forgotten that mankind is lazy and the postponement of judgment is a not uncommon way out of a difficulty. An alleged investigation may, in truth, be nothing but procrastination, a state of affairs that is peculiarly liable to develop in any service and may lead to the educated clinician developing into a collector of chits. Be not a contributor.

"In the fields of observation, chance only favours the mind that is prepared."—Pasteur.

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Before proceeding, it will be convenient to describe the physiological implications of these results. In normal blood there is presumably a state of equilibrium between the output of new cells and the death of old ones. In using the Ashby method we have to assume that the normal subject treats his own cells and transfused normal cells alike. If this is true, we can deduce the expectation of life of the red cell from the results of the transfusion experiments. These show that, to a fair degree of approximation, the destruction of the cell is due to its own ageing and not to external factors acting independently. Leaving out the intermediate syllogisms, we find that a linear decay curve implies that the red cells live for a nearly constant time, 120 days from their birth. The average life after transfusion is half this—60 days, since the transfused cells are of all ages and have already lived 60 days on the average. There is, of course, some scatter about this value, but according to our results the effect of this is not large in comparison with the experimental error.

The women present a slightly different problem. At each menstrual period a fraction of the cells transfused will be lost, and one might expect the graph, instead of being practically linear, as in the men, to be stepped (fig. 1, solid line). If the menstrual loss

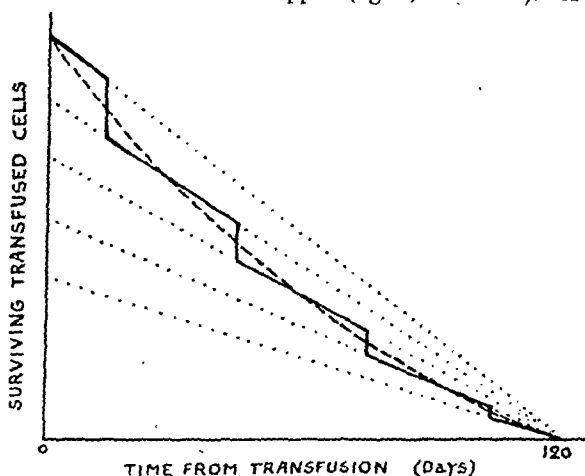


FIG. 1.—Theoretical effect of menstrual loss on the graph of survival of transfused red cells.

were sufficiently large, we might expect the periodicity to be evident on our graphs. With a relatively small loss the method is not sufficiently accurate to reveal the periodicity, but the effect will be to produce a greater curvature than that found in the males (fig. 1, dotted line). The difference between this curve and the male graph should give an estimate of the menstrual loss, if this is the only difference in treatment of transfused cells between males and females. Our female volunteers (4) did in fact give curved graphs though, as expected, the longest time of survival of cells was, as in the males, fairly sharply defined at about 120 days. Thus it seems likely that the inherent limitation of the life span is constant and that marked curvature is due to non-selective loss of blood by hæmolysis or hæmorrhage.

The calculated menstrual loss from the difference between the average of the male and female curves is 300 to 400 c.c. per period. This is, of course, extremely large. Other methods have given a loss of about 7 c.c. to 180 c.c. per period (Widdowson and McCance, 1942; Barer and Fowler, 1936). Our calculation is not really warranted by the accuracy of our methods, and the estimate may easily be in error by 50%. Also, if there had been any post-transfusion hæmolysis this would not have been separately detected, but might have accounted for a considerable proportion of the curvature in the survival graphs. Further studies are necessary to prove whether the difference between males and females is entirely accounted for by blood loss of menstruation, or whether perhaps there is an additional factor such as one related to ovarian secretion.

As far as we have gone, our work has shown that the maximum life of transfused red cells in the normal subject is about 120 days in both males and females. There is presumptive evidence that the life of any individual's own red cells, apart from the effects of hæmolysis or blood loss, is 120 days, and that the main factor determining the disappearance of any cell is its age.

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Dr. J. F. Loutit: The Ashby technique for following the survival of transfused red cells was in the past adversely criticized because of irregularities in the graphs of the red cell survival. Recent modifications and improvements have, however, resulted in a method which gives consistent and reproducible results. Extremely powerful agglutinating sera must be used; care must be taken to exclude non-specific agglutination; and the red cells of the recipient must be of high sensitivity for agglutination. Under these circumstances, as Dr. Callender has pointed out, the method gives a figure for the life-span of the normal red cell which is in agreement with that obtained recently by other methods. The subject has been summarized in two leading articles [1, 2] in British journals and one special article in the U.S.A. [3].

In contrast with Dr. Callender's account of the life-span of transfused normal red cells in normal recipients, I propose to discuss the survival of transfused normal red cells in recipients with hypochromic anaemia, Addisonian anaemia and acholuric jaundice, both congenital and acquired. I will discuss also the survival of red cells transfused from donors with Addisonian anaemia and acholuric jaundice to normal recipients. Some of these results are drawn from published works; the rest are results obtained at the South London Blood Supply Depot and are unpublished or are in process of publication. My colleagues, especially Lieut.-Colonel P. L. Mollison, have been responsible for much of the work.

Hypochromic anaemia.—In 1944 Brown, Hayward, Powell and Wits [4] studied, by the Ashby technique, the survival of transfused normal red cells in 6 cases of idiopathic hypochromic anaemia. Their results showed that the decay graph was nearly linear, indicating a nearly constant rate of destruction with an average life of the transfused red cell of just over 50 days. This corresponds with a life-span for the red cell of something over 100 days.

Very similar figures had been obtained in 1942 by Mollison and Young [5]. 15 cases of anaemia from hæmorrhage were transfused with fresh blood. The maximum survival time of the transfused red cells averaged 105 days.

It should be noted that these results only indicate the life of *normal* red cells. They give no indication of the life-span of the patients' *own* red cells.

Addisonian anaemia.—Ashby [6] herself in 1921 was able to follow to completion or near completion the survival of transfused group O red cells in 4 group A recipients with pernicious anaemia. In two of the cases elimination of the transfused red cells appeared to be complete by the 91st and 100th day respectively. In the other two, elimination was not quite complete at the 83rd and 100th day. Wearn, Warren and Ames in 1922 [7] repeated the experiment in 4 recipients with pernicious anaemia and state that the transfused red cells survived for a surprisingly long time, namely 59 to 113 days. The results of Ashby and Wearn *et al.* were obtained before the institution of liver treatment and therefore represent results in what we would now call "untreated" cases. In 1944 Brown *et al.* [4] noted one case of true Addisonian anaemia responding to liver and showed that the survival of the transfused red cells was of the normal linear type.

I have had the opportunity of transfusing with blood stored in acid citrate-glucose solution 5 cases of true Addisonian anaemia responding to liver and following the survival of the transfused red cells. Most of these cases have not been sampled sufficiently often for me to be dogmatic about the maximal or average red cell life of the transfused red cell, but qualitatively the survival was not grossly abnormal. Fig. 1 shows the graphs of the survival of the transfused red cells in the 5 cases. Even if one excludes the case given 14-day-old blood, the others given blood stored from two to seven days show a 50% survival of the transfused red cells at 31, 35, 43 and 53 days respectively (mean 40.5 days). This is rather less than the corresponding figure of 60 days obtained by Mollison and Young for blood 0 to 4 days' old in the 15 recipients with hypochromic anaemia.

On the other hand, when two convalescent subjects with mild hypochromic anaemia from hæmorrhage were transfused with blood from untreated cases of pernicious anaemia, a different graph of elimination was obtained. The pernicious anaemia donor red cells were destroyed rapidly, 50% survival occurring at about the 10th and 12th days respectively (fig. 2).

Until the discovery of the rôle of the liver principle in pernicious anaemia, the anaemia was considered to be of hæmolytic type. Subsequently, it was thought to be purely

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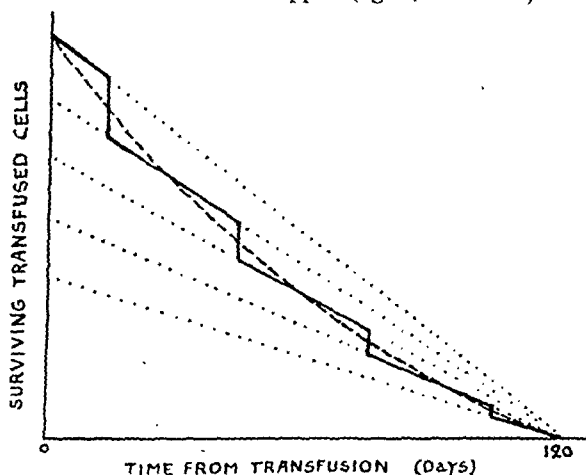


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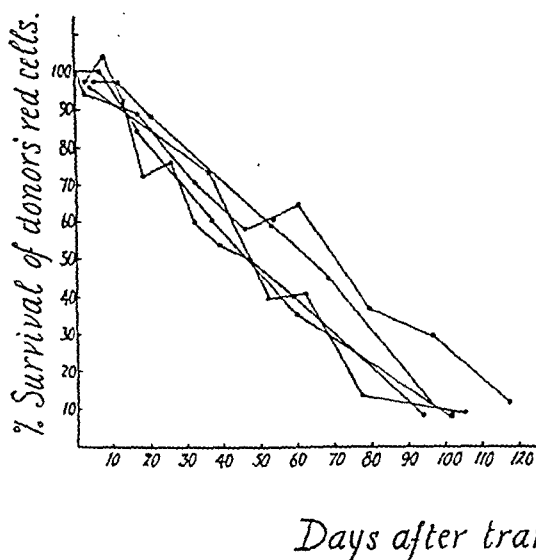


FIG. 3.

FIG. 3.—Survival of normal red cells transfused to 5 cases of congenital acholuric jaundice. (Data derived from Dacie and Mollison, 1943, *Lancet* (i), 550.)

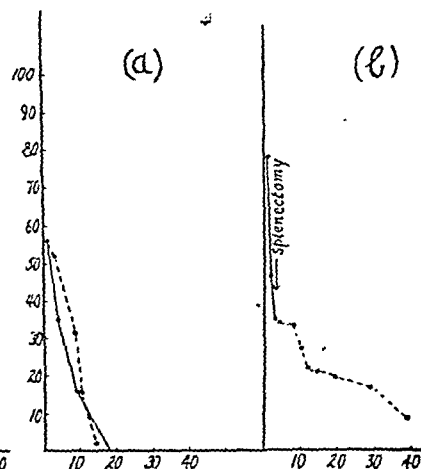


FIG. 4.

FIG. 4.—Survival of normal red cells transfused to 2 cases of acquired acholuric jaundice. (a) Continuous line—one transfusion before splenectomy. Dotted line—another transfusion after splenectomy. (b) One transfusion; continuous line represents survival rate before operation, dotted line represents the survival of the same cells after operation.

made a spontaneous and complete recovery without splenectomy and the increased red cell fragility and spherocytosis disappeared.

On the other hand, normal persons have been transfused with blood from cases of acholuric jaundice and the survival of these red cells has been followed. Fig. 5 shows

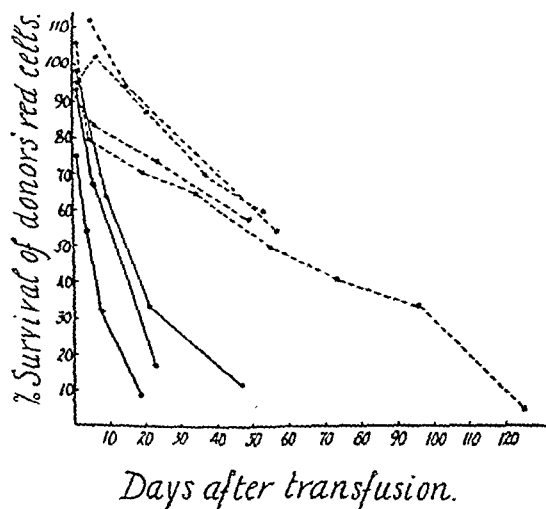


FIG. 5.—Survival of red cells from 8 cases of congenital acholuric jaundice (continuous lines) and 4 cases of acquired acholuric jaundice (dotted lines) transfused to normal recipients.

the survival of the red cells (continuous lines) of blood drawn from 3 cases of congenital acholuric jaundice. 50% survival was charted at the 4th, 13th and 15th day respectively. The survival of red cells (dotted lines) from 4 cases of acquired acholuric jaundice was substantially normal, 50% survival being greater than 50 days in all 4 cases.

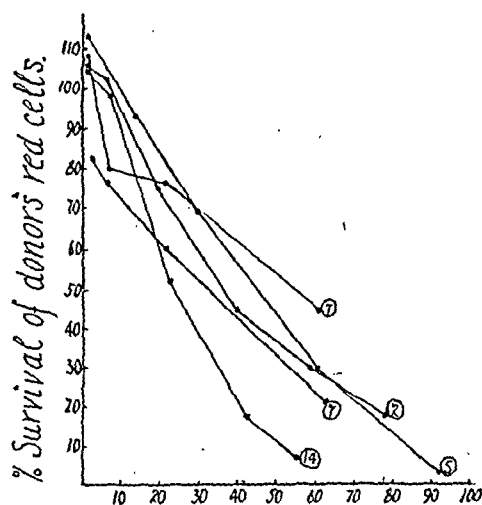


FIG. 1.

FIG. 1.—Survival of normal red cells transfused to 5 cases of Addisonian anemia. (Figures in circles indicate the age of the stored blood transfused.)

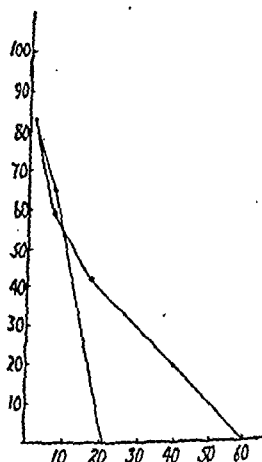


FIG. 2.

FIG. 2.—Survival of red cells from 2 cases of Addisonian anemia transfused to normal recipients.

dys hæmopoietic and that the hæmosiderosis of the organs, the hyperbilirubinæmia and the increased bilirubinoid pigment excretion were due to the failure of the body to use the by-products of red-cell destruction as occurs in normal erythropoiesis. If, however, my results of the survival of pernicious anemia red cells in convalescent subjects can be applied to the survival of the same cells in the subjects from which the blood was drawn (that is cases of pernicious anemia), then an undue hæmolysis in the peripheral blood of cases of pernicious anemia does occur and no other explanation is needed for the hæmosiderosis and the hyperbilirubinæmia. Wearn, Warren and Ames [7] did try to follow the survival of the red cells of one case of pernicious anemia in the circulation of another case of pernicious anemia, but the protocol of their results is not convincing. My conception, therefore, is that the red cells of pernicious anemia cases are discharged from the marrow with faulty protoplasm, due to the liver principle deficiency, and being faulty are as unduly susceptible to destruction in the circulation of pernicious anemia cases as in a "normal" person.

Acholic jaundice.—The term acholic jaundice is used in this country for cases of hæmolytic anemia whose red cells manifest pronounced increased saline fragility and spherocytosis. A congenital and familial form (Minkowski and Chauffard) is the common type and its existence is well established. An acquired form (Hayem and Vidal) has been postulated but not universally accepted. Our work confirms that these two types do exist and are of a different ætiology.

Dacie and Mollison (1943) [8] transfused 6 cases of the congenital type with fresh normal blood. Fig. 3 shows the results of the survival in 5 of these cases, the maximal cell life of the transfused red cells was 100–120 or more days with a 50% survival averaging 54 days.

Mollison and I have transfused with fresh blood 8 cases of acquired acholic jaundice. Fig. 4 shows the graph of the red cell survivals in two of these cases. In all these cases the maximal red cell life of the transfused red cells was grossly diminished and a 50% survival was obtained at the 1st to 28th day with a mean at 6.3 days for 10 transfusions carried out before splenectomy. In 4 of these cases 5 transfusions with red cell survival estimations were carried out after splenectomy. 50% survival was noted on the 1st to the 9th day with a mean at the 5th day—this in spite of the fact that many of the cases were markedly improved in that red cell counts and hæmoglobin figures returned to normal, though the increased red cell fragility and spherocytosis persisted. One case

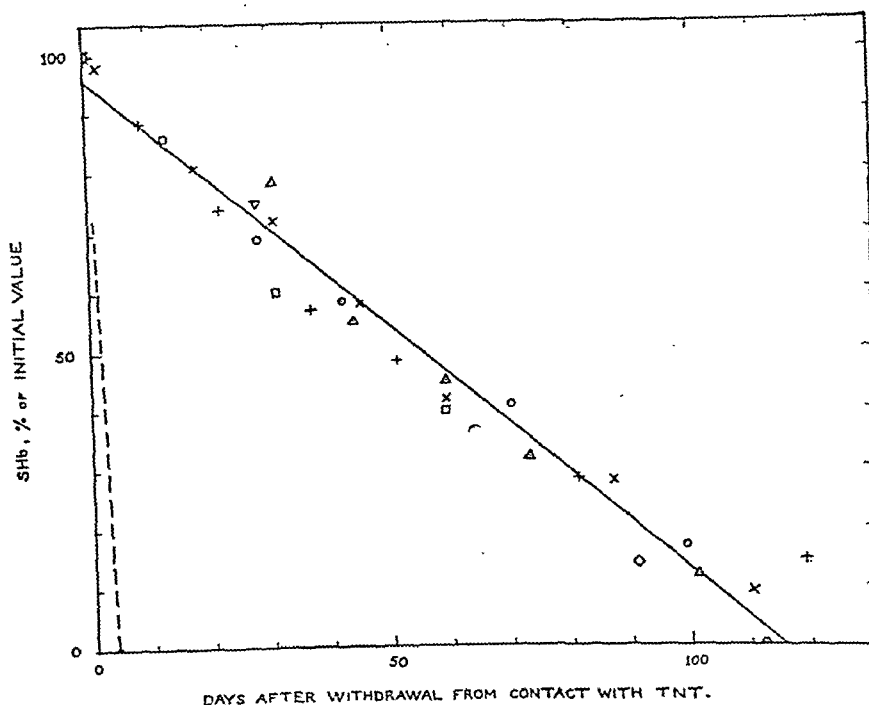


FIG. 1.—Disappearance of Sulphamoglobin (—) and of Methaemoglobin (—) from the circulating blood of TNT workers after their withdrawal from contact with TNT. The different symbols correspond to the seven workers studied.

The most serious of these assumptions is (2). SHb formation probably does go on to some extent for a few days after cessation of contact with the toxic agent, and this introduces some uncertainty into the estimate of the true starting point of the decay curve, though it probably does not affect more than the first five to ten days at the most. This matter requires further detailed study. (5) is important in comparing these results with those from other methods of estimating red cell life: however, formation of SHb within a red cell might be expected to curtail rather than lengthen its life, and this value of 116 days is considerably greater than the value of 30-50 days which has until recently been accepted.

These conclusions as to the average life span of the red cells containing SHb, and the linearity of decay curve, are in close agreement with those of Callender, Powell and Wits (1945) put forward above by Dr. Callender. Recently also Shemin and Rittenberg (1945) have studied the incorporation of the N^{15} isotope from ingested glycine into the protoporphyrin of haemoglobin, and its subsequent disappearance, and have concluded that the life span of the red cell must be greater than 100 days. Their data also are consistent with the linear decay hypothesis. It is to be hoped they will extend these experiments long enough, about 160 days, to provide a more detailed test of the above conclusions.

The differential agglutination method, employed by Callender, Powell and Wits, and the SHb method are complementary; in the former destruction of normal red cells can be followed, but not that of the subject's own cells, while in the latter the destruction of the subject's own cells is followed, though having SHb formed within them they cannot be regarded as perfectly normal. Moreover, the agglutination method is based upon a property of the red cell envelope, and the SHb method upon a property of the cell contents. It is therefore particularly significant that they should lead to a similar result for both shape of decay curve and life span.

The three approaches discussed above all give information concerning the dynamics of red cell destruction, whereas most earlier approaches to the problem of red cell life merely yielded an estimate of the average life, with no information as to the shape of

Our conception, therefore, is that the red cells of cases of congenital acholuric jaundice are abnormal due to an inborn defect of the red cell as postulated by Naegeli (1931) [9]. This would explain their abnormal survival in a normal circulation and the normal survival of normal red cells in the circulation of cases of congenital acholuric jaundice. In acquired acholuric jaundice we (Boorman *et al.*, 1946) [10] agree with Dameshek and Schwartz (1938) [11] that there is a circulating hæmolysin. This destroys transfused red cells as well as the patient's own red cells. The red cells of cases of acquired acholuric jaundice are, therefore, "sensitized". The substantially normal survival of these "sensitized" red cells in a normal circulation, though at first sight surprising, is not unique: we have been able *in vitro* to sensitize red cells which when subsequently transfused were shown to survive in a normal recipient in a fashion similar to normal red cells.

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Dr. E. M. Jope: *The disappearance of sulphæmoglobin from circulating blood in relation to red cell destruction.*—Methæmoglobin (MHb) disappears rapidly from circulating blood after the causative agent (TNT, sulphonamides, &c.) has been removed, being usually no longer detectable after about two to five days; in drawn blood kept at room temperature it may disappear in as little as twenty-four hours. This reversion to functional hæmoglobin is arrested by iodoacetate or fluoride ions and is probably coupled to the similarly inhibited reducing systems of the intact red cell, such as glycolysis (Drabkin, 1945). Continued raised levels of MHb in toxic cyanoses must be due to preponderance of toxic oxidative processes over the intracellular reducing processes. By contrast sulphæmoglobin (SHb) persists in circulating or drawn blood for many weeks. It appears therefore that the red cell has no means within it of transforming SHb, and if this is so it follows that the body can have no means of removing SHb other than by destruction of the red cells that contain it. The disappearance of SHb from the circulating blood of seven cyanosed TNT workers was accordingly studied in an attempt to follow the dynamics of this red cell destruction.

This work was made possible by the co-operation of Drs. H. K. Tucker and Helen Ramsay, and of Dr. A. J. Amor, at the time Chief Medical Officer of the Ministry of Supply, who arranged for the work to be carried out at a Ministry of Supply establishment.

The plots of the SHb levels of these workers' bloods against the time in days after their removal from contact with TNT were well fitted by the straight line (fig. 1):—

SHb (% of total pigment) = $96 - 0.83$ (days subsequent to removal from TNT contact).

This expression gives a value for zero SHb of 116 (± 5) days (fig. 1). This may be considered as an estimate of the life span of the red cells containing SHb upon the following assumptions: (1) That the intact red cell possesses no means of transforming SHb and that the body has no means of removing it other than removal of the red cells which contain it. (2) That no significant SHb formation goes on after administration of the apparent causative agent has ceased. (3) That neither SHb nor the heme part of its molecule are incorporated into new red cells.

In relating the destruction of red cells containing SHb to that of normal red cells two further assumptions must be made: (4) That the SHb is formed at random in red cells of all ages existing in the body. (5) That formation of SHb within the red cell does not prolong or curtail its life.

Section of Proctology

President—ERIC A. CROOK, M.Ch.

[July 17, 1946]

Peculiarities in the Pathology of Cancer of the Ano-Rectal Region

By CUTHBERT E. DUKES, M.D., M.Sc., D.P.H.

Pathologist to St. Mark's Hospital, London

MALIGNANT tumours which are situated partly in the rectum and partly in the anal canal often exhibit features of special surgical interest. In the first place the clinical diagnosis is often difficult, especially in the early stages of malignancy. Then the question arises as to whether a malignant tumour is a columnar-celled carcinoma extending down from the rectum or a squamous-celled carcinoma spreading up from the anal canal. This can be settled by biopsy but the microscopic examination of sections of tumours from this region not infrequently reveals an unexpected type of neoplasm. Tumours which arise at a mucocutaneous junction in any part of the body tend to be a "mixed bag" and the ano-rectal region is no exception to the rule. For all these reasons I thought it would be of interest to make a survey of the pathology of cancer of the ano-rectal region, so I have analysed the facts revealed by the pathological examination of 203 consecutive cases treated by radical excision at St. Mark's Hospital. In each case the malignant growth was situated partly in the rectum and partly in the anal canal.

SEX AND AGE DISTRIBUTION

It is well known that cancer of the rectum is commoner in men than in women, and in a series of 1,000 cases recently analysed there were 65% males and 35% females. A similar peculiar sex distribution is noticed also in ano-rectal cancers. In this series of 203 cases there were 62% males and 38% females. The average age at the time of diagnosis was 58 years, approximately the same as that for rectal cancers in general.

GROSS CHARACTERS OF PRIMARY TUMOURS

In their size, shape and other gross characters most malignant tumours of the ano-rectal region do not differ to any appreciable extent from those situated at a higher or lower level in the bowel, but occasionally a primary tumour in the ano-rectal region may be almost unrecognizable by clinical examination alone. This applies particularly to cases of colloid carcinoma associated with fistula. It is important to remember that a malignant growth may extend deeply along the track of a fistula without forming a recognizable tumour within the lumen of the bowel. Two such cases were observed in this series. In each of these colloid carcinoma had extended along the tracks of fistulae into the ischio-rectal fat without producing a recognizable tumour in the rectum or anal canal. In a third case which appeared at first to be of a similar character, the growth was found to be a teratoma. This was derived from the sacral region and produced a large mass of firm tissue containing cysts, situated between the sacrum and rectum.

So much for carcinoma associated with fistulae, but colloid carcinoma may behave in a strange way, even when fistulae are not present. In one case in this series the only visible growth was an inconspicuous linear ridge extending upwards for about an inch in the posterior quadrant of the lower third of the rectum. But though there was little to see there was plenty to feel, and when the patient was examined by Mr. W. B. Gabriel he could palpate a cord of hard tissue extending along the course of the hæmorrhoidal vessels. Subsequent microscopic examination showed this to be due to continuous permeation of the lymphatic channels accompanying the hæmorrhoidal vessels. Although the primary tumour was so small 12 out of 15 glands contained metastases. In another case of colloid carcinoma the primary growth took the form of a narrow fissure surrounded by clusters of nodules, mostly situated in the submucosa at a higher level. In this case also there was widespread permeation of all the lymphatic channels accompanying the hæmorrhoidal vessels and every lymphatic gland seen contained metastases.

HISTOLOGY OF ANO-RECTAL MALIGNANT DISEASE

Turning now from the gross characters of tumours of the ano-rectal region to their microscopic structure we find several points of special surgical interest. In the first place the surgeon wishes to know whether the growth is a columnar-celled or a squamous-celled carcinoma. The former is much the commoner. In this series of 203 tumours no less than 188, or more than 90%, were columnar-celled or adenocarcinomas which had extended down from the rectum and begun to trespass into the anal canal. Only seven were pure squamous-celled growths extending up from below. In five other cases the tumour was of mixed histology, the upper part being adenocarcinoma and the lower squamous.

Even by careful inspection of these mixed tumours one cannot recognize any difference

the decay curve. The linear decay curve implying a fixed life span for the red cell of about 120 days seems well established by these three experimental procedures. This is considerably longer than the values of about 30-50 days in man usually derived from earlier methods. The more recent work has the advantage of giving information as to the shape of the decay curve as well as an estimate of the life span, and it is difficult to explain the linear decay except in terms of non-random red cell destruction. Earlier methods based upon the assumption that an estimate of hæmoglobin breakdown could be derived from bile pigment estimations suffer from the general disadvantage that muscle hæmoglobin makes an unknown contribution to this output. Reticulocyte methods seem full of difficulties, particularly of basic definitions. It seems that the most reasonable estimate of red cell life span is given by the results of differential agglutination, SHb, and N^{15} isotope methods, published during the past eighteen months.

It would be valuable to apply the SHb method to the study of red cell destruction in animals, where the blood sub-groups are not sufficiently specific for the differential agglutination method to be employed. SHb can be formed with some certainty in the rabbit or rat by feeding with sulphur and acetanilide or phenacetin (Michel, 1938; Lemberg *et al.*, 1942), but large doses given over a short period with the intention of producing sudden high concentrations of SHb are liable to produce also another pigment, choleglobin, which may confuse the most precise attempts at spectrophotometric estimation of SHb unless suitable precautions are taken. Choleglobin has not so far been encountered in human sulphæmoglobinæmia due to TNT, sulphonamides or phenacetin, but the SHb levels are comparatively low, usually below 7% of total pigment.

In the present work SHb has been estimated spectrophotometrically. For such estimations it is imperative to work with perfectly transparent solutions, and all turbidity was removed from the whole blood dilutions by vigorous centrifugation. Turbidity can be particularly persistent in blood from cyanosed subjects, and Horecker (1944) has shown this to be due in the case of MHb to an accumulation of denatured globin within the red cells.

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tumour was found in material removed for biopsy during sigmoidoscopic examination and sent to the laboratory for diagnosis.

These six cases were scattered over the decade 1936 to 1946. The first patient was a woman aged 40 who attended the Out-patient Department of St. Mark's Hospital in 1936. A small nodular carcinoid tumour was removed from the lower third of the rectum just above the ano-rectal line, but I have not been able to get in touch with this patient again and can only say that she never returned to the hospital. The next case occurred in 1937, the patient being a woman aged 34 who was also found to have a small nodular carcinoid tumour in the lower third of the rectum. This was removed by local excision and I am glad to say that now, nine years later, her health is good and there has been no sign of recurrence. Two cases were met with in 1940, one in a man aged 40 who died one year later from other causes, the other in a woman aged 36 whom I have been unable to trace. One case was met with in 1945 and one in 1946.

The questions which have to be decided with regard to carcinoid tumours are (1) do they require any surgical treatment at all? and (2) if they are removed are they liable to recur? These questions can only be answered when a larger number of cases has been kept under observation for a longer period of time. At the present time the best advice a pathologist can give to a surgeon is to remove a carcinoid tumour by local excision and to keep the patient under observation and watch for any sign of recurrence. The real danger about carcinoid tumours is that they might be mistaken for carcinomas. This mistake is more likely to be made by a pathologist than by a surgeon because in its gross characters a carcinoid tumour does not look like a malignant tumour, whereas in its microscopic structure it does.

I have mentioned a number of peculiarities in the surgical pathology of malignant disease of the ano-rectal region, some of which are of trivial character and some of more importance. I should like as a final word to recall the four features which seem to me to be most worthy of emphasis, namely (1) the association of colloid carcinoma with a fistulous track; (2) the fact that a very small primary tumour in the ano-rectal region may have spread far and wide; (3) the observation that tumours of the ano-rectal region may be of a mixed character, the upper part being columnar and the lower squamous-celled carcinoma; (4) the occasional presence in the ano-rectal region of a carcinoid tumour of doubtful malignancy and the importance of distinguishing this from ordinary carcinoma.

A Brief Surgical Review of 201 Malignant Growths of the Ano-Rectal Region

By C. NAUNTON MORGAN, F.R.C.S.

[In *absentia* read by W. I. CAWKWELL, F.R.C.S.]

PERINEAL excision is still regarded by some surgeons as the operation of choice for growths of the rectum above which a *finger can be passed*, i.e. growths of the lower third. If this operation is to be considered a radical procedure for malignant neoplasms of the lower rectum, then those situated in the ano-rectal region should be amongst the most suitable. An opportunity has arisen for study of growths at this level of the bowel from the surgical aspect, at a time when Dr. Dukes has reviewed their pathology.

In order to obtain some concrete information regarding the best operation for eradication of ano-rectal malignant neoplasms, their surgical pathology has been studied from 201 pathological reports, scale drawings and photographs of specimens removed either by combined or perineal excision. Amongst this number were 12 squamous-celled growths, which included the mixed type already described by Dukes.

Indications for the less severe operation of perineal excision for reasons of associated disease, poor general health or as a palliative measure are not here considered, though of course these factors and especially the familiarity of the surgeon with the operation of combined excision may enter into the choice of operation.

Apart from the demonstration of lymphatic spread by dissection and microscopy of the excised specimen, accurate information regarding the suitability of the case for one or other operation is not always easily obtained. Nevertheless, an unbiased attempt has been made to assess the clinical and operative problem from the *pathological data alone*.

Combined excision is necessary for radical surgery in all growths with extensive lymphatic involvement, for those with a second malignant neoplasm several inches higher up in the rectum or where there is a submucous spread. In the large majority of instances, the degree of lymphatic implication is unknown to the surgeon; only occasionally are the full facts known before operation.

It was found on the grounds mainly of high lymphatic spread, the presence of a second growth or of submucous infiltration that about *one-half of the examined specimens* could only have been radically treated by *combined excision*.

In addition to the above findings, either alone or in association, there were other factors which called for a more radical removal than that which perineal excision can offer.

between the epithelial constituents of the growth. In two cases there were no lymphatic metastases, but in one there was evidence of venous spread. In the two cases with lymphatic metastases, some metastases were squamous and others adenocarcinoma in type.

The most probable explanation of these mixed tumours is that they are formed by the fusion of two separate malignant growths, one of which arose above and the other below the ano-rectal line. Most recent studies go to show that in their earliest phases malignant tumours are often multifocal in origin. As these small initial foci of malignant growth enlarge they fuse together making one single tumour. In these mixed tumours the parts arising above and below the ano-rectal line retained the distinctive histological features of their site of origin, although now compounded together into one single tumour.

Columnar and squamous-celled carcinomas are the commonest manifestations of malignancy in the ano-rectal region but other varieties of malignant tumour may also occur; in fact, this mucocutaneous junction may be described as fertile soil for pathological curiosities. A transitional cell type of carcinoma is by no means rare. Melanoma, lymphosarcoma, fibrosarcoma and teratoma seem to be commoner in this situation than elsewhere in the rectum or anal canal. These rarer malignant tumours often exhibit some feature which makes the surgeon suspect that he is dealing with something out of the ordinary, but this is not always the case. No doubt in their earliest phases the rarer forms of malignancy do exhibit characteristic distinguishing features, but at a later stage, especially when the surface has become ulcerated and infected, nothing but microscopic examination can distinguish sarcoma from carcinoma.

The surgical treatment of all the forms of malignancy so far mentioned is the same, namely prompt and radical excision, but what is the appropriate treatment for a tumour of doubtful malignancy, such as a carcinoid? Surgeons are of course familiar with carcinoid tumours in the appendix and it is well known that they are of a low grade malignancy, grow slowly and seldom give rise to lymphatic metastases. It is not generally known that carcinoid tumours may occur so far afield as the ano-rectal region but I have come across nine cases in which a small tumour with the characteristic histology of a carcinoid was found in the ano-rectal region or lower third of the rectum.

The special characteristics of carcinoid tumours.—They are known also as pseudocarcinomas, small-celled carcinoma or argentaffine tumours. The last name is used because it has been shown that they are derived from specially differentiated cells of the intestinal epithelium which have an affinity for silver salts. These argentaffine cells occur normally in small clusters in the cardiac and pyloric regions of the stomach and in the duodenum, and are found also in much smaller numbers in the small intestine and colon. These specialized intestinal cells often contain yellow granules which can be recognized by microscopic examination of the unstained paraffin sections and they may also be made to emit a bright yellow fluorescence. The exact function of argentaffine cells is unknown but it has been supposed that they are the source of an internal secretion. Since the distribution of argentaffine cells shows a close parallelism with the localization of the active principle against pernicious anemia it has been suggested that they may be a source of the hæmopoietic principle. Thus in twelve cases of pernicious anemia studied by Jacobson in 1939 (Jacobson, W., *J. Path. Bact.*, 1939, 49, 1) the argentaffine cells were either completely, or almost completely, absent. In two cases of sprue with macrocytic anemia an almost complete absence of argentaffine cells was also noted, whereas in other blood diseases no change was found from the normal distribution of argentaffine cells.

Carcinoid tumours derived from argentaffine cells are fairly common in the appendix but rare elsewhere. They take the form of small nodules embedded in the mucous membrane or submucosa. They are often multiple, seldom ulcerate and rarely metastasize. Even when metastases have been known to be present patients have been reported to remain alive and well for more than eight years.

Microscopic examination shows these tumours to consist of closely packed, small, round or oval cells with round, deeply-staining nuclei. The tumour cells are generally arranged in small clusters but may show a glandular arrangement. Often the tumour appears to be encapsulated but the stroma may contain smooth muscle fibres. The complete identification of a carcinoid tumour requires the demonstration of argentaffine granules in the tumour cells, but most pathologists are agreed that the histological structure is sufficiently distinctive to permit diagnosis without the use of a silver stain.

The nine cases of carcinoid tumours of the ano-rectal region which I have come across all had the form of small firm rather solid nodules situated in the mucous membrane and submucosa. They resembled small adenomas or lymphomas and did not look like malignant growths. The first three were accidental findings noticed during the routine examination of an operation specimen of rectal cancer. The question of further surgical treatment did not arise in these first three cases because the tumours were only accidentally discovered in an organ already removed from the patient, but in the other six patients a carcinoid

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or whether it seemed that both the cæcum and the appendix were involved in the same simultaneous pathological process. This decision does not create much difficulty for the previous experience of acute appendicitis teaches the surgeon to assess the condition of the cæcum which is compatible with that diagnosis.

If it were decided that the case was one of amœbic infection then the appendix was never removed but the abdomen closed perhaps with a soft corrugated drain for seventy-two hours but never around a hard tube the pressure of which might cause ulceration. Specific anti-dysenteric treatment was instituted immediately.

This routine proved satisfactory and was not varied.

I saw five cases of perforation of the cæcum or colon due to dysentery. One formed a pericolic abscess, and after drainage survived with a temporary faecal fistula. The other four died and two of them never even reached the operating theatre. Indeed with an occasional exception the condition must be recognized as uniformly fatal. The time factor is of supreme importance and wherever possible the affected loop should be brought out as a colostomy and the peritoneal cavity drained. Where the perforation occurs in a fixed portion of the colon it can only be closed and covered with omentum. The difficulty of making such sutures hold has already been emphasized. Routine treatment by intravenous infusion, continuous gastric suction and chemotherapy is added to the emetine injections, but the outlook is depressing.

The only variety of strictures of the rectum and colon following dysentery which occurred with any frequency was one situated at a constant level two inches above the anal canal. This site I assumed to be the lowest valve of Houston. Confirming this, the early cases showed a crescentic outline only later spreading to become annular and diaphragmatic and lastly extending longitudinally to involve an inch of rectal wall.

The level at which these strictures occur contrasts sharply with my observations as to the site at which the lowest lesion tends to persist in amœbic dysentery, which I found to be five and a half inches from the anal canal. The question had arisen whether proctoscopy was of appreciable help in diagnosing difficult cases of amœbic dysentery or whether sigmoidoscopy was necessary. I held the view that a sigmoidoscope was needed because from my case records the lowest site at which a solitary amœbic ulcer commonly persisted was five and a half inches above the anal canal.

This finding is obviously not an absolute one for Manson-Bahr has recorded two cases of solitary amœbic ulcer of the rectum within reach of the finger. Amœbic ulceration is frequently to be seen through a proctoscope but in such cases there is no difficulty in finding the entamœbæ in the stools and the proctoscopy is of academic interest only. I did not find that these low amœbic ulcers tended to persist. Therefore in spite of the fact that four of my stricture cases were stated to have had amœbic dysentery I am of the opinion that where a rectal stricture is attributable to dysentery it is the result of bacillary infection and it cannot be expected to respond to any specific therapy.

In my cases of amœbic dysentery two localized narrowings of the colon occurred. One was due to an amœbic granuloma, and the other to pericolicitis with abscess formation. It is clear that in either condition healing might progress to infiltration of the bowel wall with subsequent stenosis or stricture.

There now remains for comment the conditions of amœbic hepatitis and amœbic abscess and there is no clear demarcation between the two. For this reason the initial treatment is by emetine. The response is dramatic and in the majority of cases clinical recovery is complete. It is not generally agreed whether these successes include any true liver abscesses. Personally I think they do, for I have seen many cases showing all the signs of abscess formation including that of "cupping" or "tenting" of the diaphragm, but which have responded within twelve days to the emetine injections. I believe that the absorption of pus may take place if the following criteria are fulfilled: (1) The abscess is small (less than 4 oz. of pus). (2) It is situated posteriorly in the right lobe of the liver. (3) It is not secondarily infected. Obviously medical treatment cannot bring about a cure in the presence of secondary infection.

The figure of 4 oz. is empirical, and I quote it because aspiration of cases which have failed to respond to emetine usually yield more than 4 oz. of pus. I find that a higher percentage of anterior abscesses require aspiration and, following on this, a higher percentage of anterior abscesses eventually need open drainage when compared with those situated posteriorly.

In brief the treatment of hepatic amœbiasis is by medical means. Aspiration is reserved for cases in which the general condition deteriorates during the injections and those which fail to respond to the full course. Open drainage is undertaken for abscesses which recur after repeated aspiration.

Where the site could be determined by X-ray, local tenderness or bulging of the chest wall, posterior abscesses were aspirated directly over the swelling. Purely exploratory puncture was performed systematically through the lowest three intercostal spaces which

A large and bulky growth of this region will not only prevent accurate examination of the rectum and rectosigmoid above it, but furthermore the mechanical difficulties may make its removal with high division of the mesorectum impossible. Fixity of the growth and infiltration of other structures, especially when the mesorectum is short, also make adequate extirpation from below difficult. The length of bowel removed is relatively unimportant in the absence of submucous spread; it is the high division of the mesorectum that really matters. For these additional reasons, it was found that a further *one-sixth* of the cases required a combined excision. Therefore, no less than *two-thirds* of these ano-rectal neoplasms needed treatment by combined excision.

Perineal excision was considered adequate in the remaining third. These growths were either small or of moderate size with little or no fixity. There was no evidence of submucous spread and glandular lymphatic deposits were absent in all but a few and then were only slight and limited to the region of the primary growth.

Two-thirds of the malignant neoplasms under review would have brought disappointment to the surgeon who favours perineal excision, whereas he who performs combined excision whenever possible for low-lying rectal carcinomata would seldom regret his choice.

I am grateful to my colleagues at St. Mark's Hospital for their help and for the opportunity to review our more recent cases.

The Surgical Complications of Amœbic Dysentery

By K. L. JAMES, M.S., F.R.C.S.

THE following is an account of my experience of treating surgical complications of amœbic dysentery over a period of three years' service in military hospitals in India. Out of a large intake of cases only a small percentage needed to be transferred to the surgical side.

For a surgeon working in tropical climates the most difficult and anxious problem was the differential diagnosis clinically between acute appendicitis and amœbic infection of the cæcum. It is, however, a most important decision and the same problem is bound to arise in this country following the return of Service personnel from the theatres of war where dysentery is endemic.

The local physical signs in an established case are not very helpful, but Philip Howe states that early in amœbic infection of the cæcum the local signs in the right iliac fossa are already present and predominate over the generalized signs of toxæmia whereas in early acute appendicitis the general signs and referred pains eclipse any physical signs in the right iliac fossa. I regard this as a shrewd observation, and likely to prove helpful when cases are seen early.

Typical cases of acute appendicitis do occur in dysenteric subjects who may still show amœbic cysts if the stools are examined. These are suitable cases for operation and cause no difficulty; nor at the other end of the scale do those patients who are not really suggestive of appendicitis and show entamœbæ in the stools. These must receive medical treatment only. Again, a localized abscess in the right iliac fossa gives rise to no problem since the indication is always for drainage only and there is no question of removing the appendix.

There remain the many difficult cases, and I, personally, place reliance on the following points:

(1) The initial pain of appendicitis is either epigastric or diffuse around the umbilicus; that of amœbiasis of the cæcum is in the right iliac fossa or across the lower part of the abdomen.

(2) Amœbiasis must occur in a previously infected patient and therefore in a patient whose health is below par. Appendicitis, on the other hand, tends to attack a previously healthy subject. Again the history of similar attacks occurring prior to overseas service would rather point to the appendix.

(3) In amœbiasis I found that the tongue was frequently furred in patches and glazed red in other areas, whereas in appendicitis it is uniformly dirty.

My surgical specialists and I all made mistakes and in the early days three soldiers had an appendicectomy performed when the lesion was really amœbic infection of the cæcum. The first progressed satisfactorily with medical treatment. The second died of diffuse faecal peritonitis and the third had the good fortune to form a faecal fistula in the wound from which the contents of the cæcum discharged for eight months.

The truth of the matter is that the amœbic cæcum will not tolerate a purse-string suture nor will the base of such an appendix hold a ligature safely.

After these experiences I instituted in my hospitals the following procedure when a doubtful case of this nature was opened up:

Employing the minimum and most gentle handling of the bowel the surgeon should determine whether the condition of the cæcum was secondary to that of the appendix

Section of Obstetrics and Gynæcology

President—Professor F. J. BROWNE, M.D.

[June 21, 1946]

A Unilateral Krukenberg Tumour with no Apparent Primary Growth.—DOREEN DALEY, M.D., N.R.C.O.G.

A married nulliparous woman, aged 39, seen in January 1945 on account of retrosternal pain of several months' duration, not related to food and worse on bending. Neither physician nor surgeon could find any abnormality and barium swallow and follow through, chest X-ray and E.C.G. were negative.

She was next seen nine months later. Abdominal examination revealed a hard, mobile mass in the right lower abdomen rising from the pelvis almost to the umbilicus. The only associated symptom was three months' amenorrhœa following a regular menstrual cycle. On vaginal examination a normal uterus could be felt separate from the tumour which was diagnosed as a fibroma of the right ovary.

At laparotomy in October 1945 a firm tumour (8 inches across) of the ovary was found on the right side and removed. The surface was smooth and did not show any bosses. Other pelvic organs were normal and there was no ascites. Section of the tumour showed firm almost white tissue with some areas of degenerative breakdown near the hilum. There were no macroscopic hæmorrhages. *Histology*: typical Krukenberg carcinoma.

Further investigation failed to show any primary growth.

Fractional test meal, barium follow-through and enema, tests for occult blood, cholecystography, gastroscopy and sigmoidoscopy all gave negative results.

Progress.—She was given a course of deep X-ray therapy to the pelvic organs and has remained well. X-rays of the spine do not show any abnormality.

When last seen in June 1946 she had put on weight and there was still no evidence of a primary growth nor of enlargement of the other ovary.

Theca-lutein Tumour.—WILLIAM HAWKSWORTH, F.R.C.S.

The pathological specimen and preparations of a theca-cell tumour of the ovary are shown through the courtesy of Dr. Robb-Smith at the Radcliffe Infirmary.

This rare tumour was first described as a separate entity by Löffler and Priesel in 1935. Earlier literature does not appear to contain any descriptions of tumours which correspond in their characteristics to the theca-cell tumour.

Up to 1943 no more than 70 cases had been published.

The theca-cell tumour, or thecoma as it is sometimes called, is a tumour derived from the germinal tissues of the ovary and composed of elements indistinguishable from those that are present in the theca interna under normal physiological conditions of the mature graafian follicle, whether it be in its proliferative or regressive phase.

The tumour commonly occurs in the post-menopausal age-group although cases have been reported which have occurred in the adult reproductive period. It is almost always unilateral and often adherent to neighbouring organs, especially the uterus. In size it may vary from a small nodule in the ovary to a tumour of some 6 in. in diameter. The consistency of the tumour varies according to the proportion between the cellular elements and the fibrous matrix and also varies according to the presence and extent of degenerative changes. The cut surface of the tumour may be of homogeneous structure of yellowish colour, or it may be diffusely mottled with yellow areas separated from one another by whitish or greyish strands of fibrous tissue. Small necrotic areas scattered throughout the solid tumour mass as well as large cysts almost replacing the whole tumour have been described.

Microscopically the picture of the theca-cell tumour is not uniform, and even in the same specimen the cytology and the architecture show different characteristics. Geist and Gaines have given the classical description of the microscopic picture in which they say that the tumour is distinguished especially by "the presence of bundles of bright spindle-shaped cells epithelioid in appearance, distributed in a regular interlacing manner throughout the tumour, and often hyaline plaques". The presence of fat in fairly large amounts within the cells, and to a lesser extent in the surrounding connective tissue, is also stressed. Novak makes a point that in these tumours one does see from time to time areas of cells typical of granulosa cells so that he doubts the advisability of too sharp a definition between granulosa-cell tumours and theca-cell tumours, especially because they have identical endocrine effect. The mingling of epithelium and connective tissue elements in the theca-cell tumour is quite common.

Classically, the cellular elements of the tumour are described in three main groups:
(a) The cell type, which resembles the cellular elements of the theca interna of the

are to be found in the anterior axillary line. In each interspace the needle is inserted in three directions at right angles to the long axis of the body to a depth not exceeding 4 in. It is essential always to use a wide-bored needle (such as is found in the Potain set) if it is hoped to withdraw amœbic pus. Anteriorly aspiration is safe only through the costo-xiphisternal angle.

Open drainage of posterior abscesses was by rib resection with obliteration of the pleural cavity by suture. Anterior abscesses are drained through a high epigastric incision. If the level of the peritoneal reflection has been lowered by the downward enlargement of the liver a tube can be inserted at once. But if drainage is to be transperitoneal then the liver must be stitched to the parietal peritoneum.

It is well known that rupture of a liver abscess into a bronchus is frequently followed by cure but this method of drainage is uncertain and undesirable. It is not too late to aspirate or drain the liver even when the coughing up of blood-stained sputum heralds an imminent rupture.

When an amœbic abscess ruptures into the general peritoneal cavity it is sufficient to insert a suprapubic drain into the pelvis; apparently the slimy amœbic pus does not stimulate the formation of adhesions. Both my cases recovered following this procedure and neither gave rise to any anxiety.

Rupture into the pleural cavity is less fortunate probably for two reasons:

(1) The displacement of the mediastinum. (2) The tendency to diagnose pneumonia with a suspected effusion. The usual chest aspirating needle is not wide enough to withdraw amœbic pus and therefore the true state of affairs is not recognized.

Finally I was greatly impressed by the extreme wasting that occurred in cases of liver abscess. This does not mean a bad prognosis, for however emaciated the patient, his outlook is still hopeful if his abscesses are drained, provided that sufficient liver tissue is left to carry on during the recovery period, and this I find is usually so.

Air Commodore T. C. Morton: In a recent series of over a thousand cases of dysentery invalidated from the tropics, there were ten cases of amœbic liver abscess; spontaneous rupture into the peritoneum occurred in two cases, both of the left lobe of the liver, and in neither case had amœbiasis been suspected prior to laparotomy.

The importance of giving a case of amœbic hepatitis or liver abscess a full course of E.B.I. or some other potent "gut-sterilizing" amœbicide, as a follow-up in convalescence, cannot be too strongly emphasized, as otherwise reinfection from the gut of a previously damaged liver is only too probable. Emetine hydrochloride by needle alone will only cure some 7% of cases of colonic infection. I have seen two cases in the last two years where neglect of this precaution led to a reinfection of the liver, in one case with fatal results, as the second abscess ruptured into a bronchus and eventually a brain abscess developed.

Amœbic stricture of the rectum was only seen in one case for which a colostomy had been carried out in India; the case sheets described a large gangrenous slough of the rectum being passed *per anum* during the routine treatment of the case for amœbiasis. Active *Entamœba histolytica* were reported to have been found on two separate occasions in India and they were found again on his return to the U.K., both from the colostomy opening, and again in biopsy material obtained from the site of the stricture. The probable explanation in this case is that secondary bacterial infection, with a virulent organism, occurred at the site of an amœbic ulcer, leading to an intense localized inflammation which culminated in gangrene. I entirely agree with Sir Philip Manson-Bahr, that a rectal stricture due to *Entamœba histolytica per se* is almost unknown. In four cases of amœbic granuloma (amœboma) of the rectum in which, prior to treatment, it was impossible to attempt to pass a sigmoidoscope beyond the granuloma, complete resolution without diminution of the lumen followed specific emetine and penicillin therapy.

The return of thousands of Service personnel from the tropics to civil life will provide the surgeon with the additional task of excluding amœbiasis in every case of abdominal disorder, and even in hæmorrhoids and anal fistulæ. In doubtful cases I would make a plea for routine sigmoidoscopy in those cases in which the stools are negative for *Entamœba histolytica* cysts, as in 80% of cases of amœbiasis the characteristic crateriform pitting will be found (see Cropper, C. F. J. (1945), Sigmoidoscopy in Amœbic Dysentery, *Lancet* (ii), 460). I have seen an amœbic hepatitis develop following an operation for a proved adenocarcinoma of the colon. On the other hand, six cases of adenocarcinoma of the colon in this series were treated for amœbic dysentery. In two of these the growth was in reach of the examining finger. There is, therefore, a reverse side to the medal and a dual pathology must always be considered in cases of suspected amœbic granuloma refractory to treatment.

Mr. Michael Smyth, M.Ch., read a paper on "Confusion of Amœboma with Carcinoma". see *Lancet*. 1946 (ii). 376.

her own record was good. The menstrual history was normal with a mild degree of dysmenorrhœa.

On examination there were no abnormal physical findings. The adnexæ were apparently healthy and there were no palpable masses. The uterine cavity measured $2\frac{1}{2}$ in. Insufflation of the tubes was successful at a pressure of 180 mm. of mercury but no gas passed when the pressure fell below 120 mm. Biopsy of the endometrium: Secretory in type with some areas of fibrinoid necrosis and a few typical tubercles.

The patient was sent for a chest X-ray, a differential white cell count and E.S.R. before repeating the endometrial biopsy, but only the first of these investigations was carried out as she inadvertently discovered that she was a tuberculous suspect—a suggestion to which she and her husband strongly objected. The chest X-ray was negative.

She remained well until early January 1945, sixteen months later, when she complained of the onset of malaise, fatigue, cold in the head and loss of appetite. The private doctor was in attendance and early in February rigors, headaches, an unproductive cough and the clinical signs of a right-sided pleural effusion made their appearance. The patient was admitted to the Osler Pavilion under the tuberculosis officer on February 18 when she was dyspnoic, and cyanosed. Her menstrual history was still normal. There was no vaginal discharge and no clinical evidence of pelvic pathology but she still complained of a mild degree of dysmenorrhœa.

A week after admission to the sanatorium the patient became irrational, complained of severe headache and pain in the neck. A lumbar puncture revealed 100 lymphocytes per field and a few acid-fast bacilli. The condition slowly deteriorated over the next two weeks and death occurred on March 10.

Post-mortem examination.—The brain and meninges of the cord were studded with tubercles. The right pleural cavity contained an encysted effusion. The external surface of both lungs showed a moderate number of milary tubercles and the cut surfaces showed an early diffuse milary spread. There was no old-standing tuberculous lesion.

The peritoneal cavity was normal and the pelvic organs looked healthy. There were, however, some tags of omentum adherent to the posterior surface of the uterus. It was not clear whether this was an old process or a response to the recent milary spread. The fallopian tubes and endometrium showed no abnormality nor thickening; in fact the tubes were perhaps smaller in diameter than normal. The kidneys showed an occasional milary tubercle on their cut surfaces. In the mesentery at the lower end of the small intestine there was one calcified lymph node 1 cm. in diameter with several smaller hard fibrotic lymph nodes in relation to it. Microscopically there were tubercles in the fallopian tubes and endometrium although to the naked eye these appeared normal. Diffuse milary tubercles were also found in the liver, lungs, pleuræ and meninges.

The conclusions arrived at were that the original infection was the mesenteric lymph node, then the endometrium and finally a blood-stream dissemination.

During the last four years I have collected 17 cases of endometrial biopsies revealing tuberculous endometritis with no other clinically recognizable affection of the pelvic organs, and in no other case has there developed a spread of the tuberculous process beyond the pelvis, nor has any proved fatal. But on the other hand, no treatment has been successful in curing the tuberculous endometrium and in some cases, the spread to the adjacent pelvic viscera has called for surgical interference, and an operation for total hysterectomy and bilateral oophorectomy has been performed. Whilst in others, no treatment whatsoever has been given and no symptoms have arisen and there have been no unfavourable results to the general health.

Double Uterus and Bilateral Pyosalpinx.—ELIZABETH M. ROSE, M.B.

The specimen demonstrated was obtained at operation from a patient who gave the following history. In August 1938 when aged 23 and unmarried she was admitted to hospital complaining of severe pain in the R.I.F. for the first three days of menstrual periods. This had been recurring for four years and had not been relieved by appendicectomy. She was examined under anaesthesia and dilatation and curettage were carried out but no abnormality was found. Seven months later she reported again, now married and three months' pregnant, complaining of slight irregular vaginal bleeding and constant pain in the R.I.F. On vaginal examination a mass was felt to the left of the pregnant uterus. Laparotomy was performed and a double uterus was found with a pregnancy in the right horn. In the course of investigations an intravenous pyelogram revealed only one kidney and ureter which were on the left side. The pregnancy continued and was normal apart from the pain which persisted until the fifth month. The pain in the R.I.F. during menstruation was less severe after the pregnancy, but it returned and persisted, again for almost five months, when she became pregnant for the second time in 1944. Delivery and puerperium were normal as before.

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maturing graafian follicle where the cells are slender, spindle-shaped, with well-developed fibrous projections, elongated, deeply-staining nuclei and scanty protoplasm containing minute lipid droplets, or (b) cells similar to the theca interna as they appear immediately prior to rupture of the follicle, that is, ovoid or plump cells with deeply-staining atrophic fibrillary processes, roundish or ovoid nuclei and abundant fat-laden protoplasm, or (c) those cells which resemble the theca-cells after the rupture of the follicle, i.e. theca-lutein cells; these cells are polyhedral in shape, show no evidence of fibrillary projections under the usual staining methods, have central nuclei and abundant lipid in the protoplasm.

The lipid is, of course, well brought out by the usual methods of staining frozen sections of the tumour with Sudan 3 or 4, the intra-cellular lipid then appearing as bright red droplets.

The fibrous matrix of the tumour sometimes shows a picture of definite connective tissue type, alternating with areas with lack of regular arrangement. The fibroblasts are usually arranged in regular bundles and, as has already been stated, the cells of the tumour may be arranged in bundles or irregularly scattered through the matrix. The actual matrix itself is made up by fibrous projections of the cells themselves, as well as the fibroblasts. Occasionally these projections may show hyalinization.

The proportion of the cellular elements to the fibrous matrix varies considerably. The fibrous tissue gives the whitish or greyish appearance to the tissue strands in the tumour, and the fat-laden cells of the cellular elements macroscopically give the yellow colour to the tumour.

Briefly, the histogenesis of the tumour is probably best considered as arising from remnants of early mesenchymal cells, as postulated particularly by Novak and Barzilai. The symptomatology of this tumour is due, as is widely known, to the fact that it produces the female sex hormone which is responsible for changes in the endometrium, myometrium and the breast, similar to those observed in cases of granulosa-cell tumour. As a result, in post-menopausal women an irregular bleeding is the outstanding feature. During the reproductive phase, the irregularity is characterized by periods of amenorrhoea and followed by recurrent irregular periods of bleeding. All these manifestations disappear following removal of the tumour. In the differential diagnosis, owing to the fact that these tumours have been adherent to the uterus, they are frequently mistaken for fibromyomata. As a rule, this tumour is benign, but examples of proven malignancy have been described. In their treatment removal of the tumour is adequate, except in cases of malignancy where a pan-hysterectomy should be performed and followed by deep X-ray therapy.

The tumour under discussion was removed at operation from a patient aged 62, who came to hospital complaining of a blood-stained discharge for the past two months. At operation, a dilatation and curettage was performed to exclude carcinoma of the body of the uterus, and hypertrophied endometrium, characteristic of metropathia was obtained, and this, in association with a palpable small left ovarian tumour, suggested the diagnosis of a granulosa-cell tumour. The uterus and tumour were removed vaginally by Mr. Stallworthy, and the patient has made an uninterrupted recovery.

The specimen shows a left ovary enlarged to $5\frac{1}{2}$ cm. in diameter and the right ovary atrophic and normal in size for a patient of this age. The cut surface of the tumour shows little nodular patches of yellow tissue separated by strands of white or greyish fibrous connective tissue. The yellowish colour was more pronounced prior to the mounting of the specimen, but it is still sufficiently well marked to be seen without difficulty.

The endometrium appeared to be slightly thickened and the myometrium did not show any macroscopic hyperplasia. Microscopic slides show the characteristic architecture of a theca-cell tumour. The cells are varied, some spindle-shaped, others ovoid, rather plump, with roundish or ovoid nuclei and with fibrous tissue elements making up the matrix of the tumour. These are well shown in the slides stained by Masson's trichrome, and in some areas this fibrous tissue is thicker than others and gives a hyaline appearance. The cells themselves tend to scatter and extend from the epithelial masses in amongst the surrounding connective tissue. The staining does not show particularly well the fibrillary projections from the individual cells which help to make up the matrix.

This case is one of an ovarian neoplasm occurring in a patient after the menopause and giving rise to post-menopausal bleeding. The microscopical picture resembles theca interna of a physiological graafian follicle prior to ovulation, and hence the name theca-cell tumour.

Tuberculous Endometritis with Miliary Spread.—M. KATHLEEN LAWLOR, F.R.C.S.Ed.

Married woman, aged 40, attended the sterility clinic at the Radcliffe Infirmary in August 1943. She had been married five years, and had been desirous of becoming pregnant for the previous three years. Her husband, 36 years of age, was healthy and

her own record was good. The menstrual history was normal with a mild degree of dysmenorrhœa.

On examination there were no abnormal physical findings. The adnexæ were apparently healthy and there were no palpable masses. The uterine cavity measured $2\frac{1}{2}$ in. Insufflation of the tubes was successful at a pressure of 180 mm. of mercury but no gas passed when the pressure fell below 120 mm. Biopsy of the endometrium: Secretory in type with some areas of fibrinoid necrosis and a few typical tubercles.

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and constant in the same position as before. It was associated with a yellow vaginal discharge and irregular severe bleeding. On examination she was slightly febrile, T. 99·8, P. 88, and she did not look acutely ill though she was debilitated. There was tenderness in both iliac fossæ, most marked on the right side. On vaginal examination two masses could be felt, that on the left appeared to be a normal uterus while that on the right was round, firm and tender. There was slight tenderness in the left fornix. As it was considered possible that there might be a tubal pregnancy the abdomen was opened and bilateral pyosalpinx was found with the double uterus which had a single cervix. Small bowel was lightly adherent to the right tube but was separated easily, and bilateral salpingo-oophorectomy and total hysterectomy were carried out. The unilateral ureter did not cause any difficulty and the patient made a good recovery.

The case illustrates several practical points which may arise in patients with double uterus. Frequently they complain of disordered menstruation which may be irregular or painful. The condition is most often diagnosed during pregnancy, however, when the abdomen may be opened, as in this case, to exclude ovarian cyst or ectopic gestation. It is relatively common to find developmental abnormalities of the renal and genital tracts occurring in the same patient and one must bear this in mind when operating on any woman with double uterus. Another difficulty less well appreciated is that the knowledge that a patient has a double uterus may confuse the diagnosis of superimposed pelvic disease.

This patient was fortunate in having no difficulty when in labour. Commonly premature labour occurs or inertia, or the non-pregnant horn may obstruct delivery. Malpresentation, post-partum hæmorrhage and retained placenta are frequent. Perhaps the most common symptom of double uterus is habitual abortion. A patient was described who had had four early miscarriages and no normal pregnancies. On each of the last three occasions she was told that there was a tumour complicating the pregnancy. Each time she reported for treatment of the tumour after recovering from the miscarriage, but when she was not pregnant the mass could not be felt. At last she was investigated by hystero-salpingogram which explained the phantom tumour. The X-ray demonstrated clearly the same abnormality as we found in the previous case—a uterus bicornu is unicollis.

Eclampsia on the 26th Day After Delivery.—W. R. WINTERTON, F.R.C.S.

Mrs. M. D., aged 28, primigravida, was due on April 29, 1946. Pregnancy was normal, except for some giddy attacks in February. She was Rh-positive.

Three weeks before she was due she developed some œdema of the ankles but there was no albumin in the urine and the blood-pressure was 120/80. The head was engaged. She went into labour on May 2. Labour was prolonged and lasted four days, ending with a low forceps delivery. The third stage was normal.

During the puerperium her temperature remained between 99° and 100° and her pulse was rapid. On the ninth day she had a secondary post-partum hæmorrhage of fifteen ounces. She was curetted and some offensive blood clot was removed. There were no placental remains. Following the curettage she complained of headaches. On the sixteenth day some œdema of her legs was noticed. Her blood-pressure was then 120/70.

On the seventeenth day she had another slight loss. She was given a blood transfusion, but later in the day she had another post-partum hæmorrhage. Another curettage was performed but again no placental remains were removed. She was given another transfusion of two pints of blood. From then on the œdema became more marked and generalized. The œdema of the conjunctivæ was particularly noticeable and the urinary output began to drop to about fifteen ounces daily.

On May 31, the twenty-sixth day after delivery, she had a fit. During the course of the day she had eight fits. Her blood-pressure was 190/150 and the urine boiled solid. The output could not be measured as she was incontinent, but it was very small.

She was treated with sedatives and later that night when she appeared moribund was given a high spinal anaesthetic, double strength plasma and ten ounces of 5% sodium sulphate intravenously. Twelve hours later she began to regain consciousness, complained of thirst and passed thirty ounces of urine.

For the next three days she was drowsy and incontinent and the blood-pressure remained about 170/110. She then rapidly improved and by the tenth day after the fits her blood-pressure had returned to 140/90. She returned home on June 19.

On the day of the fits her blood urea was 43 mg. per 100 ml. The urine showed red cells but no leucocytes or casts.

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Section of Radiology

President—W. M. LEVITT, M.D., F.R.C.P.

[May 17, 1946]

DISCUSSION ON THE PLACE OF THE RADIOLOGIST IN THE NATIONAL HEALTH SERVICE

Dr. S. Cochrane Shanks: In considering the title of this Discussion: "The Place of the Radiologist in the National Health Service", I am at once in a difficulty, that of definition. To me the term radiologist conjures the picture of one who attempts X-ray diagnosis. To many others he is one who attempts the cure of cancer with X-rays.

Let me begin by claiming for radiologists a finger in as many pies as possible; not only in the hospital, where our place is assured, but elsewhere also: the Central Health Service Council, the Regional Hospital Board, and the Health Centre with an X-ray department.

The Central Health Service Council.—This body is to consist of 41 members, 21 of them medical. Of the latter, 6 are *ex officio*—the Presidents of the three Royal Colleges and of the G.M.C., the Chairman of the Council of the B.M.A. and of the Society of Medical Officers of Health, and two allocated to the mental services. This leaves 13 places for the representatives of the general practitioner and consultant services. Not very many—but I think we should press very strongly for at least one of these on the grounds of the importance of our specialty to all other branches, and the magnitude of our work in hospitals. Failing that, we should certainly have one representative of each of the sections of radiology on the Standing Medical Committee of the Central Council.

The Regional Hospitals Board.—The Minister has stated that the personnel of the Regional Hospitals Board will be chosen for their knowledge and administrative ability on hospital matters, and while he will seek the advice of the local authorities, the medical profession, the universities and others, the members chosen will not be sectional representatives, and so whether a radiologist is chosen or not as a member will depend on whether he has the above qualities, irrespective of his specialty. There would be no certainty, therefore, that a radiologist would be a member of the Board. In order to provide any technical advice that the Board might require, there should be appointed in each region an adviser in radiology, assisted maybe by a committee elected by the radiologists of the region. Such an adviser or committee would exercise a number of useful functions, such as having a voice on the University Appointments Committee of the region when radiological appointments were under consideration.

Again, if, as I suspect, the bulk ordering of major X-ray equipment is to be a matter for the Regional Hospital Board, who better could advise on this than a committee of radiologists of the region? I earnestly hope that the individual hospital radiologist will be given a very free choice of apparatus to suit his individual requirements, but bulk ordering will be economically attractive, and the advice of such a committee would ensure a sufficient variety in the bulk ordering to suit individual preference.

Status of the radiologist in hospitals.—There can be no doubt of the importance of the X-ray departments in hospitals: the diagnostic department deals with cases from every other department in the hospital and persistently doubles its numbers—and costs—every few years: while the radiotherapy departments become larger, more efficient and certainly fewer in number with every pronouncement of the Faculty of Radiologists.

and constant in the same position as before. It was associated with a yellow vaginal discharge and irregular severe bleeding. On examination she was slightly febrile, T. 99.8, P. 88, and she did not look acutely ill though she was debilitated. There was tenderness in both iliac fossæ, most marked on the right side. On vaginal examination two masses could be felt, that on the left appeared to be a normal uterus while that on the right was round, firm and tender. There was slight tenderness in the left fornix. As it was considered possible that there might be a tubal pregnancy the abdomen was opened and bilateral pyosalpinx was found with the double uterus which had a single cervix. Small bowel was lightly adherent to the right tube but was separated easily, and bilateral salpingo-oophorectomy and total hysterectomy were carried out. The unilateral ureter did not cause any difficulty and the patient made a good recovery.

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the radiotherapy department as an out-patient, for he will be entitled to treatment free of charge under the scheme. The differentiation in out-patients might be clearer if free treatment under the scheme was permissible only on reference from the out-patient clinics of the hospital—i.e. if the department were a "closed" one, except to private out-patients.

The case of the X-ray diagnostician is even more complicated, for so much of his work is on out-patients. Many of us are, at present, in private practice and can arrange to see our private cases—if not bedfast—in our private rooms. But in future, with the inevitable diminution in private work, and with the mounting costs of X-ray installations, few radiologists will care to face the expense of establishing private consulting rooms, and the majority will be driven to doing their private work in their hospitals. Again, the presence in the hospitals of private wards, and the principle of the open or closed department will be the deciding factors in the maintenance of private X-ray diagnostic practice.

In favour of the closed department in respect of the Comprehensive Service it is said that otherwise the departments may be flooded with unnecessary work. If everything is "free on the house" one can picture the request for a barium meal and follow through, and a barium enema; if nothing is found a cholecystography, and possibly an I.V.P. thrown in on the chance. If a patient has to pay for all that he will think twice. If it is free, the onus is thrown on the radiologist to refuse the unnecessary examination.

A more pertinent objection to the open department is in the teaching hospital, since valuable clinical material might be lost to the out-patient teaching clinics by the short circuit.

Those who favour the open department say, with considerable reason, that the family doctor is capable of handling the clinical aspect of many a case himself, and that the patient should not be forced to run the gauntlet of the out-patient clinic merely to obtain radiological evidence. In this respect, there is the recent recommendation of the Annual Representative Meeting of the British Medical Association, passed by an overwhelming majority, that general practitioners should have direct access for their patients to X-ray and pathological services, without the intervention of hospital clinicians. In some cases this may be available in health centres and cottage hospitals staffed by general practitioners, but there is no doubt that it will also be demanded in district hospitals and probably also in teaching hospitals.

Control of X-ray departments.—I should like now to insist on the principle that the radiologist should have effective charge of all the X-ray services in the institution. I have in mind a growing tendency in diagnostic departments to nuclear fission, particularly under the impact of orthopaedic neutrons. This disruption by the orthopaedists is sometimes difficult to resist, since, if their fracture clinics are situate some distance from the X-ray department, their demand for a subsidiary X-ray unit in the fracture department is very reasonable.

When they tell us that they want to have a picture of a fracture taken while the patient is under an anaesthetic, to view the pictures, and if necessary further to correct the displacement, all before the patient recovers consciousness, they are on very sure ground. The patient is entitled to that service, and we must give it, even if it means installing a unit and dark-room in the fracture clinic. But I see no objection to this arrangement if we insist tenaciously on two things: first that the subsidiary unit and the radiographer working it are part of the main department, and under the direction and control of the radiologist, and secondly, and most importantly, that every film taken in the subsidiary unit is seen and reported on by the radiological staff. It will often be after the event—it may be the next day—but this procedure gives the radiologist the opportunity of checking day by day the X-ray work done in the subsidiary department, and of drawing attention to any point in the X-ray aspect of a case missed by the clinicians, before harm is done.

Academic posts in radiology.—The establishment of university posts in any specialty should relate to the amount of teaching undertaken. Now it is true that radiologists are called upon to undertake little systematized undergraduate teaching. This is, I think, right and proper, for there is little room in the overcrowded undergraduate curriculum for systematized detailed teaching of radiology by radiologists. That in the main must be done by the clinicians at the bedside and in out-patient clinics. There is certainly not enough to warrant on those grounds alone the appointment of a university professor or reader. But, when we consider the increasing demands of post-graduate teaching, the story is very different. In London there are this year about 100 post-graduate students training for a diploma in radiology. Even if this is a peak year, there will be, I feel sure, a large number of students presenting themselves in years to come to meet the

Radiologists should, therefore, rank equally with their colleagues on the consultant staff of the hospital, with the right to sit on the medical committee, eligible to serve on the committee of management of the hospital, and to take a part in the management of our medical schools.

Organization of a radiotherapy department.—Radiotherapy of malignant disease should be conducted only in large, well-equipped and staffed centres which will tend to be in the university hospitals. In the provinces the problem is simpler than in London, where there are 12 teaching hospitals. In each of these there *must* be a major cancer centre, in order that the undergraduate students—the doctors of the future who will be responsible for the early diagnosis of cancer—may see a sufficiency of cancer cases, in the wards and out-patient clinics.

If radiotherapy has to be sent to another institution, the cancer cases will inevitably gravitate to where all the services are available. I suggest that some compromise is necessary in London by establishing a radiotherapy centre in each teaching hospital, linked together in some cases, maybe, for staffing, research and record purposes.

Organization of X-ray diagnostic departments.—There can be few working in hospital departments who are not concerned at the difficulty in keeping abreast of the ever-increasing stream of patients that pour into these departments. No sooner does one, by extension of accommodation, equipment or staff, obtain a little breathing space, than fresh increases, fresh demands threaten to engulf the department again.

Owing to the ever-increasing demands on hospitals it is seldom that the standard of work in even the good departments equals that turned out by the best of those in private practice, even if the same man be in charge of both. The remedy is clear: a sufficient number of properly trained radiologists should be employed to ensure that every case is seen by the radiologist on arrival in the department. A history should be taken, precise instructions given to the radiographer, and all films should be seen and passed by the radiologist before the departure of the patient. Then, and then only, will the quality of the work be of the highest grade.

Training of radiologists.—The criteria laid down for consultants by the Joint Committee of the Royal Colleges should apply to radiologists as to other specialists. In the initial stages of the Health Service there will be but one yardstick, the recognition by his peers that a man is a *de facto* consultant. For the future more will be necessary. One or more house appointments in medicine or surgery, a diploma course culminating in a diploma, preceded or succeeded, maybe, by taking a higher medical, surgical or radiological qualification. Finally—and here is the essence—at least three years' training as a junior in a big X-ray department, diagnostic or therapeutic. This is the only way in which to develop a first-class X-ray service for the country; and during most of his training the aspirant will be earning a reasonable living. And here may I point out a gap in our X-ray diagnostic training, in the art of radiography itself. Most of us who are established, can claim considerable experience in practical radiography in our private practice. In future, when most radiographic work is done by technicians in hospitals, there is a danger of a generation of radiologists growing up who neither position the patient nor push an exposure button. We must, therefore, plan our system of training to include for our trainees some formal and deliberate duty as radiographers in our departments.

Encouragement in research work.—As soon as our juniors have attained enough experience, they should be encouraged to undertake some work of investigation or research. The ever-increasing burden of routine work in hospital and private practice has stifled the urge to research, and denied the time for it. All this will, I hope, be changed, but only by planning the Service and training enough personnel to give leisure for this all-important aspect of our work.

Terms of service of radiologists.—Salary scales will be settled generally for all consultants: but it is appropriate to discuss whether we are to be employed part-time in hospital and part-time in private practice outside the hospital, or whole-time in one or more hospitals; and if the latter, whether we shall be allowed to see private patients in our hospitals.

To take the simpler problem first, that of radiotherapists. There seems little doubt that radiotherapy for malignant disease will in future be conducted in the main in properly organized hospital centres, and that, therefore, radiotherapists will be employed whole-time in institutions. Where his colleagues are allowed private practice in the hospital, it seems only fair that radiotherapists should have the like privilege, even if there be no segregated private section of the radiotherapy department. There may be some administrative difficulty—in deciding which patients should pay a fee. The differentiation is clear where the patient is an in-patient in the private wing, but not so clear if he attends

the radiotherapy department as an out-patient, for he will be entitled to treatment free of charge under the scheme. The differentiation in out-patients might be clearer if free treatment under the scheme was permissible only on reference from the out-patient clinics of the hospital—i.e. if the department were a "closed" one, except to private out-patients.

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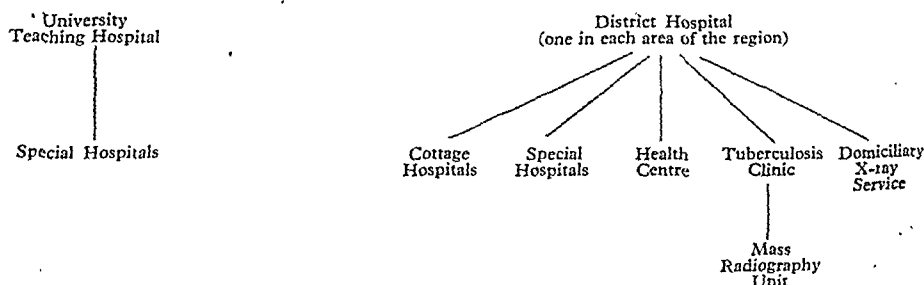
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increasing requirements of the X-ray service of the future. London University has a Professor of Radiotherapy but none in X-ray Diagnosis, and there is urgent need for at least one such of the latter in London. Indeed, two chairs in each branch of the specialty would be a great advantage from the point of view of post-graduate teaching. It is not only in London that professorships are desirable. They should be established in every university centre in the kingdom where systematized post-graduate instruction is being carried out, or where it might usefully be carried out in future.

Distribution of radiologists in the service.—I have touched on the administrative, hospital and academic status of radiologists, and on the types of appointments that radiologists might expect to hold in the future. Finally, we might also usefully consider the pattern of distribution of radiologists not only in university teaching and district hospitals, but also cottage hospitals and health centres, tuberculosis clinics and mass radiography units. Our help will also be required for domiciliary X-ray services in the patients' homes, and I hope in dermatological X-ray therapy units, working in collaboration with the dermatologist.

The diagram below indicates the broad pattern of hospital organization that will probably be adopted in the region. The university teaching hospital, with its medical school,

DISTRIBUTION OF RADIOLOGISTS IN A REGION.



If the teaching hospital acts also as a district hospital, it too should link to the ancillary services as above.

will be the academic centre and, it is hoped, the principal inspirational centre for the profession in the region. It will take its part in the regional hospital service in so far as its educational pre-occupations permit. But the backbone of the hospital service will be the district hospital centre—either one hospital or a group of linked hospitals of the district or division, with a bed accommodation of about 1,000. It has been suggested that this district centre should serve a population, on the average, of 150,000 and that there may be 10 to 20 districts or divisions in each region. To the centre should be linked the ancillary institutions as indicated in the diagram.

I have stated the thesis that X-ray diagnostic work can reach its maximum efficiency only if there is a radiologist constantly present during working hours to give personal detailed supervision to every case, and we must so design the distribution of radiologists that this requirement is met, even in small institutions where there is not enough work for a whole-time radiologist. The ideal would be to centre the radiological service of each area of the region in the district hospital (or hospitals) serving that area, in such a way that all the radiologists of the area are attached to that hospital in some capacity or other; and at this stage in the organization I think there is room for some directional control of the radiological service. There should be a director, preferably whole-time, responsible for organization of the whole X-ray service of the district. At least one senior, the X-ray director of the district, should be whole-time in the district centre—the others serving part-time in the district hospital and part-time in one or more of the ancillary institutions. The advantages of such a grouping are obvious: the benefit to all of professional contact and exchange of views and experience, the opportunity so afforded for members of the team to specialize in various branches of our work, and the avoidance of the temptation to undertake in the smaller institutions investigations or therapeutic measures which require the larger facilities of the central hospital.

The Consultant Services Committee and the Faculty of Radiologists have estimated the number of radiologists required for this service at 12 to 16 per million of the population. Recent discussions indicate that this figure may be much too low, and that more than double that number may be necessary to give the necessary detailed individual attention to X-ray work. If that should prove to be true, upwards of 2,000 radiologists may be necessary to implement the service of the future. It will obviously take many

years to train such numbers, and it must be regarded as a long-term policy, impossible to achieve with hospitals and staffs as they are. But if we are going to build a brave new hospital world let our part of it be designed with courage and vision, with proper accommodation and equipment, adequate professional and subordinate staff, real opportunity for consultation on the problems that face us, leisure for thought and for research, and, above all, freedom to investigate and treat our patients *secundum artem* trammelled only by the constructive help and criticism of our compeers.

Dr. Richard Fawcitt [*Abridged*]: The voluntary hospitals in England and Wales, 1,059 in number, provide 93,000 beds, of these one-third consist of hospitals with fewer than 100 beds.

The municipal hospitals provide 152,000 beds—78,000 of which are for general purposes, i.e. excluding infectious diseases, &c.; of these 78,000 beds 29,000 are in Public Assistance Institutions providing food and shelter for the clinically infirm and aged (*see Brit. med. J.*, 1946 (i), 653).

Numerically the non-teaching hospitals far exceed the teaching hospitals.

It is with these non-teaching hospitals that I am concerned in my remarks to-day.

It is not my purpose to deal with the past, though the present is unfortunately in many cases bound up with the past—particularly as far as accommodation is concerned—still many X-ray departments are hampered by lack of cubic space, ventilation, daylight, insufficient apparatus due to lack of room, and darkrooms little better than a cupboard.

Now as to the present. I thought it advantageous to send out a questionnaire to a colleague in each county in England and ask for his observations, preference being given to men serving more than one type of hospital, but not so in every case—I did not personally choose the individuals to whom the questionnaire was sent. The selection was made from the County Hospital list of the 1945 Medical Directory. When checking up these items in the Directory several interesting facts appeared: (1) That many hospitals are served by doctors who are also engaged in general medical

ANALYSIS OF 28 REPLIES.

Personal Questionnaire to Radiologists of Non-Teaching Hospitals.

A.—1. Are you Radiologist to more than one Hospital?	24 Yes/No 4
2. Under which of the following categories does your Hospital X-ray Practice fall?	
(a) Voluntary Hospitals:	
(i) In a large Provincial Hospital with from 200 to 400 beds or more	19
(ii) In a smaller Provincial Hospital with from 50 to 200 beds (recognized as a Teaching Centre for Nurses)	23
(iii) In a Cottage Hospital up to 50 beds	14
(b) Orthopaedic Hospitals	4
(c) Municipal Hospitals	19
d. Sanatoria, &c.	2
e. Industrial Clinics	2
B.—Do you carry out Private Practice?	
1. At your Hospitals. If so, at what terms?	26 Yes/No 2
Comments: Legion.	
2. At your own Rooms	22 Yes/No 6
C.—Do you receive any honorarium for your Hospital work?	14 Yes/No 12 (+2)
D.—Are you able to give the amount of time to your Hospital work that you consider really necessary so that every patient may receive the maximum attention?	8 Yes/No 20
E.—Do you employ Tomography or does the time factor exclude to a large extent this valuable aid to investigation?	13 Yes/No 15 (5 L)
F.—Are you satisfied that you, personally, are being adequately remunerated for the work that you are doing in Hospital?	9 Yes/No 19
If not, what alternative scheme would you suggest?	
Comments: Legion.	
G.—Are you in favour of carrying out your Private work in Hospital and NOT at your own Private Rooms?	14 Yes/No 12+2?
H.—Do you think that any form of Private X-ray Consulting Practice can survive the introduction of the National Health Service?	15 Yes/No 12+1?
In your opinion is it desirable that it should do so?	24 Yes/No 2+2?
I.—Are you satisfied in your Hospital/s	
1. With your equipment?	19 Yes/No 9
2. With your accommodation?	13 Yes/No 15
3. With the adequacy of your Staff?	
(a) Radiographic	16 Yes/No 12
(b) Secretarial	12 Yes/No 16
(c) Nursing, &c.	15 Yes/No 13
4. With the attitude of your Hospital Committees towards expenditure, remuneration and number of Staff?	19 Yes/No 9
5. With the co-operation of your colleagues in the matter of notes and investigations in other fields that would assist the Radiological conclusions...	12 Yes/No 16

Radiotherapy.

In the majority of Non-Teaching Hospitals, Radiotherapy, except for Superficial Therapy—Treatment of Skins, &c.—is seldom justified unless under the direct supervision of a member of the staff of a recognized Therapy Centre, usually a University Centre.

Normally, the Non-Teaching Hospitals, particularly the smaller ones, have no Physicist and in many cases restricted Pathological facilities. They are accordingly often not in a position to make a diagnosis let alone treat cases requiring Deep Therapy and Radium.

Do you agree with this opinion?

25 Yes/No 2
1 No Opinion.

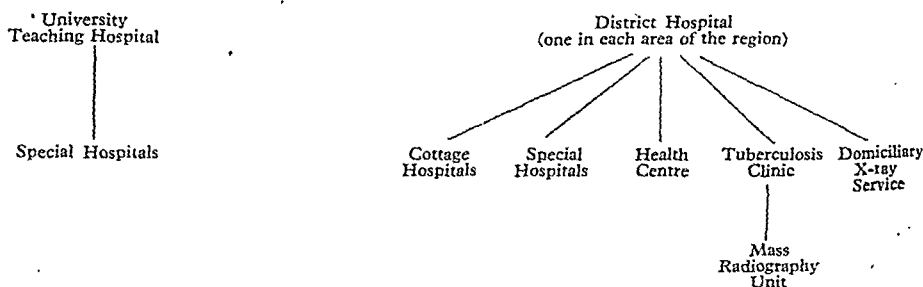
*Of the 13 who employ tomography 5 admit limited use owing of lack of time.

increasing requirements of the X-ray service of the future. London University has a Professor of Radiotherapy but none in X-ray Diagnosis, and there is urgent need for at least one such of the latter in London. Indeed, two chairs in each branch of the specialty would be a great advantage from the point of view of post-graduate teaching. It is not only in London that professorships are desirable. They should be established in every university centre in the kingdom where systematized post-graduate instruction is being carried out, or where it might usefully be carried out in future.

Distribution of radiologists in the service.—I have touched on the administrative, hospital and academic status of radiologists, and on the types of appointments that radiologists might expect to hold in the future. Finally, we might also usefully consider the pattern of distribution of radiologists not only in university teaching and district hospitals, but also cottage hospitals and health centres, tuberculosis clinics and mass radiography units. Our help will also be required for domiciliary X-ray services in the patients' homes, and I hope in dermatological X-ray therapy units, working in collaboration with the dermatologist.

The diagram below indicates the broad pattern of hospital organization that will probably be adopted in the region. The university teaching hospital, with its medical school,

DISTRIBUTION OF RADIOLOGISTS IN A REGION.



If the teaching hospital acts also as a district hospital, it too should link to the ancillary services as above.

will be the academic centre and, it is hoped, the principal inspirational centre for the profession in the region. It will take its part in the regional hospital service in so far as its educational pre-occupations permit. But the backbone of the hospital service will be the district hospital centre—either one hospital or a group of linked hospitals of the district or division, with a bed accommodation of about 1,000. It has been suggested that this district centre should serve a population, on the average, of 150,000 and that there may be 10 to 20 districts or divisions in each region. To the centre should be linked the ancillary institutions as indicated in the diagram.

I have stated the thesis that X-ray diagnostic work can reach its maximum efficiency only if there is a radiologist constantly present during working hours to give personal detailed supervision to every case, and we must so design the distribution of radiologists that this requirement is met, even in small institutions where there is not enough work for a whole-time radiologist. The ideal would be to centre the radiological service of each area of the region in the district hospital (or hospitals) serving that area, in such a way that all the radiologists of the area are attached to that hospital in some capacity or other; and at this stage in the organization I think there is room for some directional control of the radiological service. There should be a director, preferably whole-time, responsible for organization of the whole X-ray service of the district. At least one senior, the X-ray director of the district, should be whole-time in the district centre—the others serving part-time in the district hospital and part-time in one or more of the ancillary institutions. The advantages of such a grouping are obvious: the benefit to all of professional contact and exchange of views and experience, the opportunity so afforded for members of the team to specialize in various branches of our work, and the avoidance of the temptation to undertake in the smaller institutions investigations or therapeutic measures which require the larger facilities of the central hospital.

The Consultant Services Committee and the Faculty of Radiologists have estimated the number of radiologists required for this service at 12 to 16 per million of the population. Recent discussions indicate that this figure may be much too low, and that more than double that number may be necessary to give the necessary detailed individual attention to X-ray work. If that should prove to be true, upwards of 2,000 radiologists may be necessary to implement the service of the future. It will obviously take many

Section of Psychiatry

President—G. W. B. JAMES, C.B.E., M.C., M.D., D.P.M.

[June 11, 1946]

The Depersonalization Syndrome

By H. J. SHORVON, M.B., B.S., D.A., D.P.M.

[This paper has been written in collaboration with Dr. J. D. N. Hill, Dr. E. Burkitt, and Mr. H. Halstead.]

INTRODUCTION.

In his classical paper "On Depersonalization" in 1935 Mayer-Gross [1] commented on the meagre literature despite the widely scattered distribution of the syndrome. The term "depersonalization" was first used by Dugas [2] in 1899, to name a syndrome originally described by Krishaber [3] in 1872 under the title of cerebro-cardiac neurosis. The definition of the term as conceived by different writers tends to be a descriptive one, each stressing particular aspects according to his special approach. Thus Schilder [4] in 1914 says: "The individual feels totally different from the previous being; he does not recognize himself as a person, the outside world appears to him foreign, the 'self' does not behave any more in the former way." Oesterreich [5] views it more from the standpoint of affect, thus: "There is a diminution or complete disappearance of feeling, the individual's sense of living is gone, the central life sense is checked." Janet [6] observes that "depersonalization takes place when the individual does not recognize the maximum of consciousness and of reality, and depersonalization is nothing else but an internal perception of the disturbance in the function of reality, or else a dissolution of attention and therefore a release of automatic activity." Wiersma [7] defines depersonalization as "a suddenly occurring rapidly passing state in which everything in the environment is perceived vaguely and indistinctly. The complaint is not infrequently heard that everything, though well perceived, is with difficulty recognized. The voices of others, and also of the person himself, are plainly heard but not recognized. It is as if the perceptions are duly accomplished, but the associations which they arouse in normal circumstances are not formed. The patients complain that they cannot think properly, that they cannot reflect; they feel dull and dazed, and the examination shows they have difficulty in answering questions".

Krapf [8] says of the syndrome: "The individual expresses himself as strange, his perceptions insufficient, his feelings empty, his thoughts shallow without relief, his acts automatic. It has been remarked for long that the strangeness is a faraway perception.

or surgical practice; (2) that where a doctor is radiologist to one hospital only he usually is of the above type, or else has a whole-time radiological appointment at that particular hospital; (3) that most radiologists on my list serve several hospitals; (4) that a number of men appear to serve far too many hospitals and cannot possibly do their job efficiently; (5) that several serve hospitals in more than one county, some in more than two.

I can foretell some difficulty in dealing with this problem when regionalization comes along—if it does.

When we get above two hospitals, and in some cases in two hospitals also—the number of beds served is in the region of 600 more or less.

Where one man runs two hospitals the question of holidays is so difficult to solve that it usually results in no holidays at all.

The type of hospital is fairly general and varied. Note the lack of radiologists in orthopaedic hospitals and sanatoria—these tend more and more to be dependent for the interpretation of their radiographs upon their own staff, with its limited knowledge.

With regard to the final question on radiotherapy, the answers are overwhelmingly in favour of having a first-rate staff and well-organized radiotherapy departments in our hospitals, specially adapted for this purpose.

On the whole the non-teaching hospitals have put up a good performance and have done, and are doing, their best.

They are *not* in many cases fulfilling the ambitions of their radiologist: (a) Through lack of staff—chiefly medical—and inability of radiologist to give necessary time; (b) shortage of apparatus in many cases; (c) lack of accommodation; (d) lack of funds to provide these; (e) lack of co-operation of colleagues in other fields.

Let me stress that this state of affairs does not apply to the teaching hospitals and to many of the non-teaching hospitals. In the case of the small hospitals perhaps the answer lies in the principle that some of us provincial radiologists have tried to follow out. In the smaller hospitals we cannot attempt to handle all the special cases, e.g. neuro-radiology, because, in the first place, we do not see enough of them. We must be prepared to send these cases to larger centres, university centres or other special centres where they can be adequately handled by a team.

I should like to end with a plea for Refresher Courses, and for frequent meetings to promote not only interest and study in radiology but also to foster a spirit of co-operation and wide understanding amongst us.

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and Olsen and Ruby [33] state that anosognosia may arise in three distinct situations, namely a lesion of the thalamus, a lesion of the thalamoparietal peduncle, or a combination of motor cortical lesion and an interparietal lesion. Anton [34] in 1899 described a condition of failing perception which consisted of Babinski's anosognosia and the lack of recognition of blindness and deafness. In Gerstmann's syndrome [35], or finger agnosia, the body schema is affected by a focal cerebral lesion in one hemisphere only, the hemisphere concerned with the individual finger. This occurs in lesions of the angular gyrus. The patient's psychic condition is good, but may be disturbed for a time. Bender and Kanzer [36] describe a dreamlike state of unreality occurring in a parieto-occipital tumour, with disturbance in the perception of forms, and spatial order of objects, and in the orientation of the patient in space. Russell Brain [37] describes three cases of a distinct form of visual disorientation resulting from a lesion of the posterior half of the right cerebral hemisphere, and characterized by an inattention to the left half of external space. Significant contributions to the problem of disorder of the body image in psychiatry have been made by Gurewicz [38] on the "interparietal syndrome" which is characterized by two types of phenomena; disorders in the body image, and metamorphosis. Bychowski [39] reviews the study of the body image and says the Vienna School attempted to take into consideration the psycho-analytical view-point. This view-point attributes to narcissistic motives the fact that the patient refuses to admit to himself that his extremity is missing. The phenomenon of anosognosia has been related by Pözl [40] and Schilder with the role of repression. It must be pointed out that in all the above neurological conditions, the condition is a *sign* of loss of function which can only be demonstrated by testing. In depersonalization, however, the condition is a *symptom* complained of by the patient; the difference therefore is between a sign and a symptom, or difference between a disorder at the level of behaviour and a disorder at the level of experience.

Clinical Findings.

This investigation is based on a series of 66 cases recently examined and treated in the Sutton Emergency Hospital neuropsychiatric unit, and in the psychiatric out-patient departments of four London hospitals. There was no age selection, but we have excluded severe psychotics and involutional depressives, although we know the symptom is common amongst them. We have confined ourselves almost entirely to cases in which depersonalization is either the presenting symptom, or plays a leading part in the symptomatology, or is a clinical entity, in all of which the patients understand the morbid nature of their state. The value of our selection is that we have a clear picture of the symptoms studied and many cases will fit into no other diagnosis than the depersonalization syndrome. Practically all cases were leading a comparatively normal life prior to the onset. In the history-taking, particular attention was paid to the patient's description of the symptoms, often supplemented by a written account of his attitude to the symptoms. Care was taken as far as possible to avoid leading questions, and a verbatim account of the patient's statements was taken at the interviews. Each case had a full psychiatric investigation, and physique, personality development and intelligence were assessed. Miss J. M. Moore, psychiatric social worker, supplied social and family histories in most of the cases, visited the homes and interviewed near relatives. Special investigations carried out included the Rorschach test in 18 male and 22 female cases, the electroencephalogram was recorded in 23, and Miss Elizabeth Bennett did a series of imagery type assessments. The 66 cases comprise 46 females and 20 males. The youngest age of onset was 10, the oldest 38; the average age of onset in women being 24.5 years, and in men 23.5 years. 20 cases began under the age of 20, 30 cases between the ages of 20 and 30, and 16 cases from 30 to 40. A quarter of the cases had a sudden onset of depersonalization between the ages of 15 and 19. It is impossible to give a composite survey of the duration of symptoms as the majority of the cases are still depersonalized. Some cases have had recurrent attacks of varying duration, others have remained persistently depersonalized for many years with or without marked fluctuations in its course. Thus one patient has had recurrent attacks for twenty-six years, another for twenty-three years, and 7 patients have been persistently depersonalized for seven years. 2 cases have up to date a persistent duration of symptoms of nine years; 1 of eleven years; 2 of thirteen years. One patient has had a fluctuating course over twenty-seven years, and another in a similar way over twelve years. It must be emphasized that affective disorder could not be regarded as primary in these cases. The physique of patients varied in type, but the majority are of asthenic or athletic habitus. A point of possible interest in the previous medical history is that 9 cases had rheumatic fever in childhood and many others had recurrent attacks of tonsillitis and bad throats.

All descriptions of the symptom fall naturally into those of changes of the self, or changes of the outer world. In the latter, attempts to classify cases into those experienc-

Objects seem different, colours weaker, food without flavour." Again Lange [9] gives a good description. He says: "The feeling of belonging to one's own body is lost. The patient feels like an automatic machine, like a statue. The sound of his voice, his face in the mirror seems strange to him. His mental pictures are shadowy. His perceptions do not awaken a feeling of reality, his actions are mechanical, without the feeling of will. Thoughts come and go without personal effort. The patient feels like an apathetic spectator without connexion with his own perceiving and doing."

As Mayer-Gross points out, when depersonalization is referred to one generally includes in addition to changes of the self, changes in the environment, called "derealization" by Mapother.

Depersonalization can occur in any morbid psychological reaction and is common in manic-depressive states, schizophrenia, obsessional neurosis and involuntional melancholia, but also occurs in anxiety states and hysteria. It is seen in states of altered consciousness and occurs in encephalitis lethargica [10, 11, 12], in epilepsy [13], intoxication, delirium, hypoglycæmia and exhaustion. It has been described in organic conditions such as brain tumour and trauma [14], athetosis, hypoparathyroidism, carbon-monoxide poisoning [15] and mescaline intoxication [16].

The mechanism of depersonalization has been approached from psychological and neurological view-points, and a diversity of theories have been advanced by descriptive psychiatrists, psycho-analysts and neurologists. Mayer-Gross has suggested that it is a dysfunction of cerebral origin, and is a preformed functional response of the brain. He also suggested that modern physiological methods should be used to elucidate the mechanism, and this we have attempted to do. We can only briefly refer to some of the important psycho-analytical views. Gordon [17] broadly describes the syndrome as a converted representation of hidden or repressed emotional consciousness by a special determination. Schilder [18] stresses the shift of the libido in these patients, and its partial concentration on a scrutinizing tendency. Nunberg [19] believes it to represent a loss of libidinal attachment as a result of physical punishment and a narcissistic wound. Sadger [20] states it may be an attempt to escape psychic castration, and Searl [21] regards it as an attempt to escape psychical and physical punishment by possessing the immunity of inanimate objects. Freud [22] makes his first mention of the subject of estrangement and depersonalization in 1937, noting two general characteristics, first, that they belong to the defence mechanisms tending to hide something from the ego—estrangement, or denying a portion of the ego—and secondly, that they are rooted in the early past of the individual. Feigenbaum [23] points out that depersonalization is seen to serve as a means of defence—namely, by projection. Oberndorf [24] has written a series of papers on the subject, stressing four successive mechanisms: parental identification; erotization of thought; identification of such thinking as a characteristic of the parent of the opposite sex; and repression. Wittels [25] also suggests that the important mechanism is the use of identification in the formation of personality. He says: "It seems to me that the cause of depersonalization is an unusually great number of phantom figures, leaving the ego in such a position that it cannot decide which one of the figures has to be acknowledged as its representative. In terms of the libido theory we could say insufficient ego libido is invested in any one of these phantoms. Hence they are all grey and colourless, surrounding a perplexed and swaying personality. In all cases of depersonalization under my observation something was wrong in the infantile relation between the patient and the father. It does seem to me as though the super-ego is responsible for the disintegration of personality by condemning all of the phantoms without exception as unreal."

Neurologists have attempted to explain the syndrome in terms of local cerebral function, although no pathological changes are found in cases of depersonalization as we understand them. They point out the close association of depersonalization and the phenomena of *déjà vu*, and also the connexion between disturbances in the "body schema" and its representation in the cortex [26, 27, 28, 29]. This "body schema" or "body pattern" is the concept which a person has of the image of his own body, or that of another, and the spatial relations of the parts of the body to each other. The body image is intimately associated with the cerebral cortex especially the inferior parietal, marginal, and angular gyri, and in the case of focal lesions loss of the body image may occur, but the patient may not be aware of its disturbance; nor need it interfere with motor function. Such lesions do not necessarily affect projection tracts, but involve association systems and cause genuine disturbance of the psyche [30]. Thus, in anosognosia, first described by Babinski [31], in which condition an individual is unaware of his own disease, there is a specific defect in body image. Defects in body image are common in neurological and psychiatric conditions. Barkman [32] showed that the hemiplegic anosognosia described by Babinski, was due to a lesion of the right thalamus;

the pregnancy. 6 cases followed operations (with anaesthesia), and a few followed some days after minor injuries to the head. One pregnant woman became depersonalized whilst looking at some pictures in the National Gallery, after she had been taking massive doses of abortifacients and had given up the idea of successfully inducing an abortion. Another pregnant woman stated that it followed the taking of salicylates, and another patient was taking 15 grains of thyroid daily to reduce her weight before the onset of symptoms.

Unlike most psychiatric conditions some patients find that when they concentrate the symptom recedes and when they relax it returns; as one patient says: "I concentrate and get things back a little, but the strain is too strong and as soon as I relax everything has gone again. I felt an attack coming on after my third confinement, but beat it this time by keeping my mind working." One young man had been almost continuously depersonalized for eight years. He said he felt worse when relaxed and all right if occupied. He supposed he was the only person who would welcome, for instance, a fire, as the excitement would relieve his symptoms. The happiest period of his life was when the Gestapo were after him and he was hiding or moving about, living on wheat ears and dry meat. He was symptom-free then.

Our data fully substantiates the attitude taken by Mayer-Gross that it is possible to find support for a variety of theories about depersonalization by selecting suitable descriptions. He describes under the heading of theories from incomplete data the following:

TABLE I.—TOTAL CASES 66.

	No. of cases		No. of cases
Altered time perception ...	22	Loss of feeling accompanying action	30
Altered space perception ...	21	Disturbance of memory ...	6
Lack of affect ...	22	Altered range of consciousness ...	20
Bodily change ...	45		

(1) Altered experience of time (Lewis [41]). (2) Changes in perception of space. (3) Lack of feeling. (4) Subjective experience of bodily change. (5) Loss of the specific feelings which accompany action (Loewy [42]). (6) Disturbances of memory. (7) Increased self-observation (Schilder). (8) Changes of clearness and range of consciousness and it seemed to us that equally we might add (9) Disturbances of autonomic function.

Professor Aubrey Lewis has pointed out that time consciousness "is an aspect of all conscious activity; it is essential to all reality. In *déjà vu* there is a brief inability to actualize the present, which in consequence is projected into the past". Of time disturbances in depersonalization he says: "They illustrate many of the outstanding features of the disorder; the inability to evoke the past readily or clearly, to distinguish the present from the past or future; there is paradoxically the increased quickness with which time passes though it seems to drag along, the seeming remoteness of the recent past, the unconfirmed feeling of inability to judge the length of time. In depersonalization there is a change in space and time consciousness which may be expressed in various forms."

We have found altered experience of time in 22 cases and they fit in well with Professor Lewis's observations. One patient stated: "The times have gone. I can remember but there is nothing in that. The day is gone and it is empty. Time is gone, is a blank. I have been here ten days and it seems I've been here no time at all." Another patient said: "When I do anything it seems such a long time ago. If I do anything in the morning it seems like weeks ago. Time does not mean anything; it seems long drawn out."

Twenty-one cases described changes in perception of space. For example: "Everything around me was far away and tiny", or "When I walk the ground seems to be high up. If I put anything down it seems to come towards me", or "The garden simply receded and looked like a scene on the stage."

Twenty-two cases described lack of affect. "The emotional part of my brain is dead. My feelings are peculiar, I feel dead. Whereas things worried me nothing does now. My husband is there but he is part of the furniture. I don't feel I can worry. All my emotions are blunted."

Forty-five cases showed subjective experience of bodily change. "Queer sensations connected with my breathing. I am conscious of not breathing like other people and feel myself on occasions taking deep breaths which don't come easily. My head and my breathing is in a muddle."

Thirty cases seemed to show loss of the specific feelings which accompany action. "If I laugh when somebody makes a joke it is automatic. There just doesn't seem anything there." "I sing but I can't get the feeling of happiness. I lie in bed and get up and

ing a loss, those a change, and those an addition to the outer world, showed that addition is very rare, and that the same patient would at times speak as if the environment had something missing in it, and at others as if the quality of his perceived experience had changed. Again there was no clear distinction to be drawn between derealization and depersonalization. Whereas we have not found derealization without depersonalization, the reverse occurred in a few cases. In the majority, the patient would complain at different times in terms of altered experience of self, or of the outer world, but would lay emphasis on one or the other. In our attempts to elucidate differences of this type we have recorded verbatim patients' descriptions of their symptoms, but in practice it becomes clear that patients have the greatest difficulty in communicating their experiences. Such communications do not readily lend themselves to objective divisions of this sort. This may be due either to the complex nature of the experience, or possibly to the fact that it is difficult to put into words. This may explain why the best descriptions are given by the most intelligent patients.

Fear, and the experience of being misunderstood, or being thought insane, have led many patients to suppress this symptom, and to complain of accompanying somatic changes. Such patients are often diagnosed as affective disorders.

Out of the 66 cases, 61 had a sudden onset, 3 cases were doubtful and in 2 the onset was gradual. Intelligent people describe the onset of the experience of unreality in a number of different ways, or in a composite way which would fulfil the criteria of more than one theory. Thus one patient said: "Suddenly everything was strange, unreal, and I was a different person." Another said: "Everything suddenly went black. It was as though something had snapped, and from then on things seemed different." A few random descriptions include: "I suddenly felt peculiar." "I suddenly felt I was dead." "It was as if my brain turned right over, and it left me with a dreamy confused and bewildered feeling." "I suddenly could not think what I was saying. I could not focus. I was talking to someone and yet I was there and not there." "I wondered whether I looked the same. I kept repeating to my husband: 'Am I the same? do I look the same?'" "I was walking down the stairs one day when half my mind seemed to go. I kept looking at things to see if anything went back to normal, to see if they were in their original perspective."

In some cases the symptom is first of momentary duration, and then may recur at intervals, lasting longer each time, finally becoming stationary; or the condition may continue unvarying. The symptom frequently sets up a panic state, and it is common for patients to complain from that time of fears of insanity, of impending death, and particularly of fears of going out alone, and inability to travel. The initial onset is frequently accompanied by overbreathing or difficulty in breathing, a feeling of faintness without an actual faint, and numerous somatic symptoms of anxiety.

An interesting observation is the frequency with which depersonalization begins during a period of relaxation following prolonged fatigue or psychological stress or both. In our series it is commonly found to commence after such conditions, for instance when on holiday, or in the change over from an arduous or unpleasant job to a lighter or more congenial one, or in soldiers during leave, after demobilization, or awaiting return home from abroad. One patient had a very worrying time over the question of marriage which she did not desire, and the attack began a week after her fiancé was sent overseas; whilst another patient who had badly missed her soldier-husband had an attack when he was home on leave. One patient, after being evacuated from home for years, had tramped the streets of London for weeks trying to find a place in which to live, and the attack came on four days after resting at her sister's home. Another patient had had little rest during the "blitz" and became depersonalized soon after evacuation to the country. Other cases followed broken engagements, and one after the termination of a homosexual love-affair of many years' duration and of a very unsatisfying nature. An obsessional individual with fears of dirt contracted pediculi pubis, and he went through severe stress; he became depersonalized during a period of intense relief following the cure of his skin trouble. An obsessional young woman who was very harassed by a nagging mother-in-law, and worried by her infant's thrush, became ill after she left for her own home and the baby's condition cleared up. A highly intelligent, strongly obsessional man of 31 who obtained a first-class honours degree in economics after intensive study in the evenings—he was a wage earner by day—became preoccupied with abdominal pains due to a spastic colon and mucus colitis. His condition was complicated by attacks of migraine and after an unsuccessful course of analytical treatment he was admitted to hospital in a tense agitated state. He responded well to physical treatment and rest, but became depersonalized a month later. 8 cases followed within two to six weeks of parturition. In these cases there had been severe psychological and physical stress during

the pregnancy. 6 cases followed operations (with anæsthesia), and a few followed some days after minor injuries to the head. One pregnant woman became depersonalized whilst looking at some pictures in the National Gallery, after she had been taking massive doses of abortifacients and had given up the idea of successfully inducing an abortion. Another pregnant woman stated that it followed the taking of salicylates, and another patient was taking 15 grains of thyroid daily to reduce her weight before the onset of symptoms.

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Bodily change ...	45		

(1) Altered experience of time (Lewis [41]). (2) Changes in perception of space. (3) Lack of feeling. (4) Subjective experience of bodily change. (5) Loss of the specific feelings which accompany action (Loewy [42]). (6) Disturbances of memory. (7) Increased self-observation (Schilder). (8) Changes of clearness and range of consciousness and it seemed to us that equally we might add (9) Disturbances of autonomic function.

Professor Aubrey Lewis has pointed out that time consciousness "is an aspect of all conscious activity; it is essential to all reality. In *déjà vu* there is a brief inability to actualize the present, which in consequence is projected into the past". Of time disturbances in depersonalization he says: "They illustrate many of the outstanding features of the disorder; the inability to evoke the past readily or clearly, to distinguish the present from the past or future; there is paradoxically the increased quickness with which time passes though it seems to drag along, the seeming remoteness of the recent past, the unconfirmed feeling of inability to judge the length of time. In depersonalization there is a change in space and time consciousness which may be expressed in various forms."

We have found altered experience of time in 22 cases and they fit in well with Professor Lewis's observations. One patient stated: "The times have gone. I can remember but there is nothing in that. The day is gone and it is empty. Time is gone, is a blank I have been here ten days and it seems I've been here no time at all." Another patient said: "When I do anything it seems such a long time ago. If I do anything in the morning it seems like weeks ago. Time does not mean anything; it seems long drawn out."

Twenty-one cases described changes in perception of space. For example: "Everything around me was far away and tiny", or "When I walk the ground seems to be high up. If I put anything down it seems to come towards me", or "The garden simply receded and looked like a scene on the stage."

Twenty-two cases described lack of affect. "The emotional part of my brain is dead. My feelings are peculiar, I feel dead. Whereas things worried me nothing does now. My husband is there but he is part of the furniture. I don't feel I can worry. All my emotions are blunted."

Forty-five cases showed subjective experience of bodily change. "Queer sensations connected with my breathing. I am conscious of not breathing like other people and feel myself on occasions taking deep breaths which don't come easily. My head and my breathing is in a muddle."

Thirty cases seemed to show loss of the specific feelings which accompany action. "If I laugh when somebody makes a joke it is automatic. There just doesn't seem anything there." "I sing but I can't get the feeling of happiness. I lie in bed and get up and

ing a loss, those a change, and those an addition to the outer world, showed that addition is very rare, and that the same patient would at times speak as if the environment had something missing in it, and at others as if the quality of his perceived experience had changed. Again there was no clear distinction to be drawn between derealization and depersonalization. Whereas we have not found derealization without depersonalization, the reverse occurred in a few cases. In the majority, the patient would complain at different times in terms of altered experience of self, or of the outer world, but would lay emphasis on one or the other. In our attempts to elucidate differences of this type we have recorded verbatim patients' descriptions of their symptoms, but in practice it becomes clear that patients have the greatest difficulty in communicating their experiences. Such communications do not readily lend themselves to objective divisions of this sort. This may be due either to the complex nature of the experience, or possibly to the fact that it is difficult to put into words. This may explain why the best descriptions are given by the most intelligent patients.

Fear, and the experience of being misunderstood, or being thought insane, have led many patients to suppress this symptom, and to complain of accompanying somatic changes. Such patients are often diagnosed as affective disorders.

Out of the 66 cases, 61 had a sudden onset, 3 cases were doubtful and in 2 the onset was gradual. Intelligent people describe the onset of the experience of unreality in a number of different ways, or in a composite way which would fulfil the criteria of more than one theory. Thus one patient said: "Suddenly everything was strange, unreal, and I was a different person." Another said: "Everything suddenly went black. It was as though something had snapped, and from then on things seemed different." A few random descriptions include: "I suddenly felt peculiar." "I suddenly felt I was dead." "It was as if my brain turned right over, and it left me with a dreamy confused and bewildered feeling." I suddenly could not think what I was saying. I could not focus. I was talking to someone and yet I was there and not there." "I wondered whether I looked the same. I kept repeating to my husband: 'Am I the same? do I look the same?'" "I was walking down the stairs one day when half my mind seemed to go. I kept looking at things to see if anything went back to normal, to see if they were in their original perspective."

In some cases the symptom is first of momentary duration, and then may recur at intervals, lasting longer each time, finally becoming stationary; or the condition may continue unvarying. The symptom frequently sets up a panic state, and it is common for patients to complain from that time of fears of insanity, of impending death, and particularly of fears of going out alone, and inability to travel. The initial onset is frequently accompanied by overbreathing or difficulty in breathing, a feeling of faintness without an actual faint, and numerous somatic symptoms of anxiety.

An interesting observation is the frequency with which depersonalization begins during a period of relaxation following prolonged fatigue or psychological stress or both. In our series it is commonly found to commence after such conditions, for instance when on holiday, or in the change over from an arduous or unpleasant job to a lighter or more congenial one, or in soldiers during leave, after demobilization, or awaiting return home from abroad. One patient had a very worrying time over the question of marriage which she did not desire, and the attack began a week after her fiancé was sent overseas; whilst another patient who had badly missed her soldier-husband had an attack when he was home on leave. One patient, after being evacuated from home for years, had tramped the streets of London for weeks trying to find a place in which to live, and the attack came on four days after resting at her sister's home. Another patient had little rest during the "blitz" and became depersonalized soon after evacuation to the country. Other cases followed broken engagements, and one after the termination of a homosexual love-affair of many years' duration and of a very unsatisfying nature. An obsessional individual with fears of dirt contracted pediculi pubis, and he went through severe stress; he became depersonalized during a period of intense relief following the cure of his skin trouble. An obsessional young woman who was very harassed by a nagging mother-in-law, and worried by her infant's thrush, became ill after she left for her own home and the baby's condition cleared up. A highly intelligent, strongly obsessional man of 31 who obtained a first-class honours degree in economics after intensive study in the evenings—he was a wage earner by day—became preoccupied with abdominal pains due to a spastic colon and mucus colitis. His condition was complicated by attacks of migraine and after an unsuccessful course of analytical treatment he was admitted to hospital in a tense agitated state. He responded well to physical treatment and rest, but became depersonalized a month later. 8 cases followed within two to six weeks of parturition. In these cases there had been severe psychological and physical stress during

Miss Elizabeth Bennett gave imagery tests to 16 cases. She reports that the majority of these patients are predominantly visualizers, a finding which is of no significance, since this is by far the most frequent type in the general population. A few patients have complained of loss of visual imagery, and in two cases this is considered to have been genuine and specific. In the remainder, however, it was found to be a part of a general difficulty in concentrating attention; to a marked visualizer, such a difficulty would naturally be expressed in terms of loss of visual imagery. Investigations of the reality sense showed that in the majority of cases where the external world appears unreal, it appears so equally in all sense modalities. In two cases, however, visual perceptions seemed to be especially affected, things heard or touched retaining their reality quality. Tests for body image showed that the majority of patients did not locate themselves in any particular part of the body. Among those who did, the head was the most favoured site. There were some exceptionally vivid visual images of structural damage to the brain, which damage was equated with irreparable loss of the self.

Our patients use the terms "as if" or "as though" showing there is no delusional content, but remarks are made at times which suggest the basis for the formation of secondary delusions, hallucinations, and ideas of reference in obviously psychotic patients. Thus one patient stated: "I have a feeling I am speaking very loudly to people and they are looking at me in a surprised sort of fashion. This is a silly idea to explain, but I have the feeling that people, even when I am not speaking, are looking at me in surprise" so illustrating the beginnings of ideas of reference. Another patient similarly failed to return to work because her workmates commented on her appearance. "I pick up things said by others. I take notice of all nonsense although I know it is silly." Another patient showed the germs of delusions and hallucinations. Something inside him said "Hope is gone". He felt he was a strange monster and had distressing somatic symptoms such as things flailing about inside him and others which were indescribable".

Hysterical phenomena such as overbreathing, hysterical tetany, or difficulty in swallowing may be a prelude to depersonalization; they may be intermingled with symptoms of depersonalization or it may be expressed as such symptoms, and it is relatively common for hysterical behaviour, and rarely psychogenic amnesias, to follow improvement of the depersonalized state.

TABLE II.—TOTAL CASES 62.

		<i>Previous personality.</i>					
		No. of cases	%			No. of cases	%
Obsessional traits...	...	56	88	Hysteria	...	13	20
Anxiety	...	35	55	Migraine	...	24	38
Hypochondriasis	...	8	13	Déjà vu	...	39	62
Abnormal father relationship		32 out of 48 cases					

As already stressed the type of case we are presenting shows the depersonalization syndrome as a more or less distinct clinical entity with a sudden onset in non-psychotic patients. A study of the previous personality in these patients is revealing. 56 out of 63 patients (or 88%) showed an obsessional personality, 27 (or 43%) mildly so, and 29 (or 46%) markedly so. The great majority of cases therefore tend to be over-conscientious, rigid, ruminative individuals with phobias and a tendency to compulsions. 35 out of 63 (or 55%) have always been anxious individuals. 8 patients (13%) showed previous hypochondriasis and 13 (20%) had hysterical trends. During the illness 45 patients (71%) exhibited an obsessional state, and 37 (59%) were depressed. It is surprising, despite the alleged significant relationship between migraine and obsessional personality, that 24 out of 63 (38%) suffered, or suffer, from migraine and there is an immediate family history of migraine in 13 cases (21%). 10 cases in the series gave a history of migraine in the family although not affected themselves. An interesting clinical observation is that many cases when questioned state that the migraine attacks ceased with the onset of depersonalization. Previous writers, such as Oberndorf [43] and Schilder [44], stressed the close association between the phenomena of *déjà vu* and depersonalization. 39 cases out of 63 (62%) in our series experienced this, the majority frequently. An actual history of depersonalization in the family is rarely obtained, but striking cases do occur. In only 2 cases were such histories obtained. There is a history of allergy in some form in one member of the family in 11 cases, and in only 2 cases is there any family history of chorea. 13 patients out of 63 give a personal history of allergy.

In the mechanism of depersonalization the father relationship has been stressed by psycho-analysts. An investigation of our cases shows that of the 48 cases on which we could obtain information about the father-child relationship, 32 patients were fearful and frightened of their father in childhood, and used various expressions such as harsh, strict, bad-tempered, without affection, when talking about this parent. 16 patients stated

feel all numbed but I do my work." "I am still here now and talking to you and touching things but not in the same way as before I was ill."

Six cases showed disturbances in memory. "If I go outside I shall not remember you. I have clothes but I can't memorize them, unless I go and strain and look at them."

Self-observation although common enough is occasionally expressed in a striking manner: "It is as if I was looking inside my head instead of outside. I seem to be thinking always inside of me instead of out of me." "I suddenly seemed to see myself. I am conscious of my hands."

Twenty cases complained of changes of clearness and range of consciousness. "I just sink into a kind of unconsciousness. I am just conscious enough to know that things are going on around me but nothing seems to register." "I am in a daze." "I seem to be looking through a mist." "Muzzy sensations." "In a dream." "Dopey." "In a fog"—are common expressions.

Disturbances in autonomic function are common in our series. Frequent expressions are: "I have difficulty in breathing and an empty feeling in the pit of the stomach." "A choking sensation and difficult to breathe with giddiness as if I am going to faint." "My stomach shakes."

The number of cases and quotations illustrating the disturbances in function integrating the personality have been obtained from the case records, and must obviously represent minimal percentages of the total cases. Individual cases describing some of these disturbances probably experience some other changes but have omitted to mention them at interviews, particularly so because of the care we have taken to avoid leading questions. A few of our cases show disturbances in all the tabulated features. Having presented selected data from patients' accounts which support well enough the theories of depersonalization mentioned, we now wish to emphasize that the complaints are not restricted in this way. The actual expression of the symptom is undoubtedly dependent on the intelligence, temperament and cultural background of the patient.

The range of actual experience of depersonalization varies from mild changes in "self" to the extreme of feeling two persons, and it is worth quoting some verbatim accounts. A young woman stated: "I can't think it is me. I used to feel I was someone. It never entered my head I was someone else, as though I had changed. I must be someone, I am someone, everybody else feels someone, but I am not myself. I suddenly felt I am in half, there is two of me. The two halves of my body felt they had become apart."

As Mayer-Gross pointed out, cases of severe bodily depersonalization may be unaccompanied by derealization. One young man of 20 said: "I can't seem to find my actual self. I feel as though my deliberations are those of a public body or corporation rather than those of a person. I used to say 'we' rather than 'I'. It is as though I had transcended personality, as if 'myself' had receded to an image which I regarded objectively, and which is not identified with the whole of me". Another patient stated: "I am not living in a world at all. When looking in a mirror I have to keep telling myself the reflection is mine. It's like looking at another person."

Depersonalization of parts of the body, especially head or limbs, are very common. Descriptions include: "The top of my head is popping and buzzing and then it seems to go all numb." "I could look down at my hands and see them writing but they don't seem to belong to me."

Patients frequently describe the experience of something between their eyes and the outside world—"curtain", "blind", "fine wire netting", "fine mesh", "glass wall" are some of the expressions used, and it is common to complain of circles before the eyes. This is bound up with descriptions of experience of change in the outside world that is, derealization. "If I am walking along, round things look distorted and something different. When walking it is as though there is nothing there. There seemed to be some kind of barrier between me and the others, it was almost as if I were under water and I could just see distorted shapes around me. In fact, the people and things around you seem as unreal to you as if you were only dreaming about them." Or "I look at people, the sun, the flowers, everything looks different." "Through the eyes I look out at a world that might be a picture of the world, of objects vaguely unreal till I touch them—a mirrored reflection."

Some patients complain vividly of their inability to visualize. "When you walk into a room you can see a woman there but you have also a mental picture of the room and that's what I don't have. I can see the furniture, but I can't make a mental picture." "One of my chief worries is the fact that I cannot make any mental picture. If I shut my eyes, for instance, it is like a complete blackout, there are no thoughts coming through at all."

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that their childhood was satisfactory or that their father was good to them. This preponderance of an unsatisfactory parent-child relationship is significant.

Rorschach Findings.

We discussed various ways of obtaining supplementary data on personality by psychometric methods. It was finally decided to use the Rorschach test.

TABLE III.—RORSCHACH TEST.

Aspects underemphasized			
	No. of cases	%	No. of cases
Colour responses... ..	10	48	Narrow range of content ...
Kinaesthetic responses ...	29	73	Failure—one card or more ...
Texture responses ...	20	50	

Aspects overemphasized			
	No. of cases	%	No. of cases
Form responses	32	80	Rare and minute details ...
Anatomical-sexual responses	13	32	Orderly-rigid approach ...

18 cases (45%) have a lack (imbalance) of colour in the colour-kinaesthetic ratio, despite the under-emphasis of the latter.

Protocols were taken, individually, from 18 men and 22 women, all unselected. The ages ranged from 20 to 44 (average 28) for the men, and 15 to 48 (average 30) for the women. The spontaneousaneous record was followed by the usual inquiry, but there was no "Testing of Limits".

Looking at the results, it is that of constrictive controls a whole with all its interrelated parts, the general impression being one of rigidity. Some of the signs were: A kind associated with the obsessive-compulsive personality (in some cases), over-emphasis on rare or excess of concepts determined purely by shape (in many failures to respond (25% of cases) and minute details (30% of cases), the high percentage of responses, the orderly or rigid way the ratio of whole (intellectual) to kinesthetic (more restricted range of the subject-matter (in dealing with the location categories, and regard to accuracy of form, and there was a 45% of the cases). Many were meticulous, over-thoroughly before surrendering them, with a distinct compulsion to deal with the conflicts in the personality-balance, could be seen reluctance. Indecision, internal answers, e.g. "It could be a bat or a butterfly"; or indecision directly in the frequent answer it a . . . ?" or "It is a . . . isn't it?"

The group as a whole is intellectually superior as shown by the average IQ of 110.

The personality-balance on a global view of the test indicates two indices to be taken into account: (a) the ratio of human concepts, and (b) the ratio of animal movement to texture responses, is said to reflect conscious tendencies, and the latter the more inclinations not fully accepted by the individual. It also indicates he is at present heading. On the conscious level the group shows but this is overruled by the second index, from which we infer the of the group are introverts, 17% ambiverts, 18% extraverts, while tendencies, the basic introverted trends being masked by pseudo-extraversion.

Movement responses are inadequate and the ratio of animal to human this area is more than 2 to 1, a balance normal up to puberty but generally. Thus, we may infer emotional immaturity, an unwillingness fulfil the adult role. The question is left open as to whether the immaturity or a regression due to psychic trauma.

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Whereas the group produced 45% of its responses to the three brightly colored composite reaction times were over-long for these cards, and many cases of preference for the grey cards as being less of a strain. This is held to indicate that patients were attracted towards reality but found difficulty in dealing with it. The two extremes—of whole answer on the one hand and partial answer on the other—were over-emphasized in comparison with the middle ground.

The two extremes—of whole answer on the one hand, and tiny or rare detail other—were over-emphasized in contrast to the more obvious areas of the L there was a general shortage of popular responses. This suggests a lack of aw everyday matters.

Anxiety is display

Anxiety is displayed notably through cases of the cases as again form is still dominant of the "Blood" or "in inter" type.

through the different Rorschach
and more especially the form
the colour and the shading
in check, with occasional
hostilities, found
ving project

coming up for the kill, lions tipped out of an airplane, caterpillar impaled and split open, a horrible beetle that you squash and it cracks." Responses emphasizing the horrible or evil nature of the things seen were fairly common.

Four cases remarked on a feeling of being drawn down or falling towards the blots, and staring eyes were common.

32% of the cases were scored for significantly high anatomical responses, indicating, in a lay group such as this, body preoccupations.

Card VI of the Rorschach Test produced abnormal signs such as long reaction times, low productivity, failures, &c. As this card is known to be weighted for sex, we may infer sexual disturbance as a noticeable characteristic of the group.

Perseveration was another sign of constriction noted; in most instances it was recognized by the patients.

In conclusion, we may say that the Rorschach pattern of this group of patients has little in common with that found in organic cases, but has most of the features indicative of psychoneurosis with a high quantitative measure of maladjustment. This is expressed mostly in a formal, compulsive attitude to life, with the more positive emotions tightly repressed or denied.

E.E.G. Findings.

Electro-encephalographic investigations can provide us with data relevant to the problems of depersonalization from a number of different points of view. First, a disorder of attention, either to visual perceptions or to visual imagery, would be related to the failure of the alpha rhythm to block to stimuli. The equal presence of alpha rhythm on the two hemispheres, having a mainly post-central distribution and blocked by visualization, is a demonstration of the normal resting function in the visual association areas. Failure of blocking is seen in normal non-visualizers, and in many patients with reversible or irreversible deterioration of attentive capacity from any cause. In the 23 cases of depersonalization examined in this series, all showed normal blocking of the alpha rhythm to opening the eyes. The alpha rhythm in one case, showing a poor response to this, blocked normally when told to look. In this instance, as in others tested, the alpha blocking during mental arithmetic was normal. We were able, in one case, to demonstrate the return of the alpha rhythm while the eyes were open when the attention was diverted, first to auditory stimuli, and then to tactual stimuli. These findings provide evidence of a normal physiological functioning of the cortical cells, and their inter-connexions in those brain areas serving visual perception and in particular those in Vogt's area 19.

The second point of interest is the comparison of the group as a whole with the normal population and related psychiatric groups. 13 of the 23 cases examined had minor abnormalities in the E.E.G. compared with the standards of normality at present accepted. This percentage abnormality (over 50) is extremely high for any non-organic group with the exception of the chronic psychotic mental hospital population. The figure is about twice as great as that found by most workers for any mixed psychoneurotic group. While 5 of the E.E.G. + group had received convulsive therapy, none of the E.E.G. - group had done so, and no doubt this is a contributory factor in making for E.E.G. abnormality. However, when one excludes these, about 35% are still abnormal, and this is still an unusually high figure. The age factor is also probably significant, although the numbers are too small for certainty. In the whole group the ages ranged from 19 to 42 but the average for E.E.G. + cases was 26 years, and for the E.E.G. - cases 32 years. The significance of the age factor is enhanced by the fact that the 6 E.E.G. + cases showing instability of rhythms to overbreathing were all at the young end of the age range, the average being 23 years.

Examination of the abnormalities themselves shows them to be of the minor sort. Only one case had a focal abnormality and he was known to have had migraine. The group was heterogeneous, in that some had slow rhythms, some fast, and others fast and slow. None, however, showed paroxysmal activity and none rhythms at less than 4 c/sec. In none was any relationship to the epileptic group found, nor any evidence of an organic process such as is given from the presence of a focus or from the characters of the wave forms. The increase of slow rhythms during overbreathing (6 cases), and their reduction by breathing CO₂ and amyl nitrite (2 cases) is in conformity with the findings in other cases in whom a physiological dysfunction can be inferred with greater certainty. Repeated examinations made on a few cases during the illness and after recovery showed the patterns to be constant in appearance. Reduction of slow activity by chemical action had no effect on the symptom, and for these reasons, as well as from general principles, there is no reason to believe that the E.E.G. abnormalities are in any way directly related

to the mechanism of depersonalization. It would seem that they must be regarded in the same light as the E.E.G. abnormalities in the case of the psychoneurotic cases. The abnormalities are minor deviations from the normal pattern, heterogeneous variations which are more frequent in the younger patients, and an expression of constitutional or developmental variation from the normal.

Response to Treatment.

Scant attention has been paid in the past to the question of treatment in cases of depersonalization, particularly in non-psychotic cases. In involuntal depression and schizophrenia the symptom tends to disappear with the improvement in the psychosis. In the group with which we are concerned we find, generally speaking, that most physical methods of treatment may improve the affective state but seem to have little or no effect on the unreality feelings. Psychotherapy and analytical methods, of course, have been used extensively; but in stubborn cases show little result. We have attempted an evaluation of results and have classified them according to the responses to convulsion treatment, continuous narcosis, benzedrine, epanutin, vasodilators and abreaction techniques especially with the use of ether, or a combination of cardiazol and ether. On one case Dr. Dalton Sands has had a prefrontal leucotomy performed. Psychotherapy has been used in all cases in conjunction with the physical methods employed.

E.C.T.—39 cases have been treated with a course of electro-shock therapy. This is a treatment commonly used, and it is important for the results to be carefully assessed. The number of treatments given varied from three to fourteen. One of the cases states his depersonalization started after a course of E.C.T. Of the remaining 38 cases only 2 lost their depersonalization, 4 were improved, 1 was temporarily improved, there was no change in 22 cases, and 10 patients stated they were worse. Thus, 32 out of the 39 patients were unchanged or worse after the treatment. Of the 32, 5 were less depressed, 10 slightly improved, and 17 remained the same. Of those that recovered or were much improved, 2 were post-puerperal, 2 were recurrent depressives, and 2 were hysterics with depression.

There is, therefore, little or no place for the use of E.C.T. in the treatment of depersonalization where it is a clinical entity. The treatment is of value for endogenous depressions, but in such cases it is the depression which is relieved and the depersonalization clears up with it.

Continuous narcosis.—15 cases had a full course of continuous narcosis with sodium amylal and paraldehyde. 7 showed no change, 4 appeared worse, and 3 were relieved of their tension with no change in depersonalization. One patient recovered. He was a case of recent onset with marked obsessional and anxiety features. The results on the whole are poor.

Benzedrine and epanutin.—39 cases had a course of treatment with benzedrine 10 to 20 mg. daily. 27 showed no change. 10 cases were improved, generally slightly and only in their affect; one was much improved, but there was a probability that epilepsy complicated this illness, and another case showed improvement in derealization but not in depersonalization. Epanutin in increasing doses was tried with 23 patients, 18 without effect and 5 showed slight improvement. An epileptic patient had her fits controlled by benzedrine and epanutin, but she had a sudden onset of depersonalization when under treatment.

Vasodilators.—These had little or no effect. 13 cases were treated with 50 to 100 mg. t.d.s. of nicotinic acid for weeks without effect. Intravenous injections of 10 c.c. Afenil (CaCl_2 -urea) were given daily to 7 patients for a fortnight. There was a slight relief of anxiety in 2 cases, and no change in the remainder.

TABLE IV.—RESPONSE TO TREATMENT.

	Total cases	Results			
		Recovered	Improved	No change	Worse
E.C.T.	39	2	4	23	10
Contin. narcosis	15	1	0	10	4
Benzedrine	39	0	2	37	0
Epanutin	23	0	5	18	0
Nicotinic acid	13	0	0	13	0
CaCl_2 -urea	7	0	0	7	0
Insulin comas	6	0	0	6	0
Leucotomy	1	1	0	0	0
Ether abreaction	14	4	7	3	0

Ether abreaction.—It occurred to Dr. William Sargant and myself [45] that abreaction ~~ether~~ ^{other} means of excitation might be attempted in the group.

There were some interesting results in the 14 cases tried. 4 patients lost their depersonalization dramatically and have remained well. One was a female of 29 who was depersonalized for six months and becoming agitated and depressed. She was abreacted over an incident in a bus which mounted the pavement. Great excitement was deliberately stimulated till the patient went into a state of temporary "collapse" [45] and when she came round there was immediate and lasting loss of depersonalization. Before this she had had a course of E.C.T. without effect. The other case was a man of 44 who had suffered depersonalization for six years and was intensely anxious. E.C.T. had failed to relieve him. He had a phobia of dirt and was abreacted over an attack of pediculi pubis which had preceded his depersonalization. He showed tremendous affect. The first abreaction ended in violent excitement, but as he did not reach the point of collapse he was immediately abreacted again. This culminated in a short period of stupor, with lasting relief of symptoms. A third patient who became depersonalized three weeks after her first child was born abreacted violently over her confinement experiences with good effect. The fourth patient was a young man who was predominantly derealized; his symptoms cleared after a general abreaction. Among other cases of this group are, one obsessional patient of 20 persistently depersonalized since the age of 13 showed little affect under ether, but he reported "minutes of normality" for some days; and an agitated obsessional woman of 24 on coming round showed rapid fluctuations of unreality and normality. A girl of 20 in the W.R.N.S. was abreacted over an incident in a classroom when she was unable to answer a question and became depersonalized. She became very excited and lost her depersonalization for several hours. She relapsed and was again abreacted with only momentary improvement, and then became anxious and dissociated. Another patient of 25 who had been depersonalized for eleven years, following a moderate ether abreaction, lost his symptoms of derealization with diminution in intensity of depersonalization. This was only temporary. A patient who was profoundly depressed and depersonalized also showed a momentary loss of the symptom, whilst 2 others stated the next day that they felt something had lifted, and were relieved but still depersonalized. 3 patients failed to show any excitement under ether and there was no change. Anxious patients tend to respond; depressed patients remain apathetic.

Cardiazol.—Cardiazol fits were reported by Schilder [46] to produce some useful results. We have not been able to investigate this finding adequately but 1 case had no result from 5 fits and 2 others, who had one and two fits respectively, showed no change. The injections were given after E.C.T. had failed. The result in a fourth patient, however, was very interesting. He had been depersonalized for three years and was given an intravenous injection of 6 c.c. of cardiazol whilst he was in a light stage of insulin coma. This was insufficient to produce a fit but he showed very marked twitching and generalized excitation. When the hypoglycemia was subsequently interrupted by intravenous glucose he said he "felt lighter and everything appeared normal. He could see the trees, &c., as they used to look". He remained well and some days later said: "Everything is bright, as if I have come out of a dark room into a bright room. Something has lifted—gone. I used to feel as if I was in two, but now I am whole." This result may have some similarity to the good results obtained by the induction of excitation under ether.

Modified insulin.—Modified insulin produced physical improvement in most patients with increase in weight, but had no effect on depersonalization. *Deep insulin* comas in 6 cases similarly produced no benefit.

Leucotomy.—One patient had prefrontal leucotomy performed. She suddenly became depersonalized in 1938, three weeks after a confinement, followed by depression and loss of interest in her baby and family. She remained in this state, and entered a mental hospital in 1942 where she was given five cardiazol treatments without benefit. Later she had a course of ten E.C.T.s and a course of sleep treatment again without improvement. In 1944 she was in another mental hospital and treated unsuccessfully with thyroid extract. She remained persistently depersonalized with marked emotional blunting, and said she felt empty and dead, automatic, time meant nothing, and that nothing came from her mind. Her personality was obsessional. She was admitted to hospital under Dr. Sands. A course of analytical treatment produced no change, neither did deep insulin comas and she became agitated, tearful and emotional. In March 1945, when aged 39, with a history of seven years' continuous depersonalization, a leucotomy was performed by Mr. Wylie McKissock. For a time there was little change except for an easing of tension, but later she began to lose her depersonalization. She continued to complain at intervals of depression and lack of feeling towards her family but there was a marked improvement nine months after the operation. Except for some irritability and temper she has now

to the mechanism of depersonalization. It would seem that they must be regarded in the same light as the E.E.G. abnormalities in the case of the psychoneurotic cases. The abnormalities are minor deviations from the normal pattern, heterogeneous variations which are more frequent in the younger patients, and an expression of constitutional or developmental variation from the normal.

Response to Treatment.

Scant attention has been paid in the past to the question of treatment in cases of depersonalization, particularly in non-psychotic cases. In involutional depression and schizophrenia the symptom tends to disappear with the improvement in the psychosis. In the group with which we are concerned we find, generally speaking, that most physical methods of treatment may improve the affective state but seem to have little or no effect on the unreality feelings. Psychotherapy and analytical methods, of course, have been used extensively; but in stubborn cases show little result. We have attempted an evaluation of results and have classified them according to the responses to convulsion treatment, continuous narcosis, benzedrine, epanutin, vasodilators and abreaction techniques especially with the use of ether, or a combination of carbiazol and ether. On one case Dr. Dalton Sands has had a prefrontal leucotomy performed. Psychotherapy has been used in all cases in conjunction with the physical methods employed.

E.C.T.—39 cases have been treated with a course of electro-shock therapy. This is a treatment commonly used, and it is important for the results to be carefully assessed. The number of treatments given varied from three to fourteen. One of the cases states his depersonalization started after a course of E.C.T. Of the remaining 38 cases only 2 lost their depersonalization, 4 were improved, 1 was temporarily improved, there was no change in 22 cases, and 10 patients stated they were worse. Thus, 32 out of the 39 patients were unchanged or worse after the treatment. Of the 32, 5 were less depressed, 10 slightly improved, and 17 remained the same. Of those that recovered or were much improved, 2 were post-puerperal, 2 were recurrent depressives, and 2 were hysterics with depression.

There is, therefore, little or no place for the use of E.C.T. in the treatment of depersonalization where it is a clinical entity. The treatment is of value for endogenous depressions, but in such cases it is the depression which is relieved and the depersonalization clears up with it.

Continuous narcosis.—15 cases had a full course of continuous narcosis with sodium amytal and paraldehyde. 7 showed no change, 4 appeared worse, and 3 were relieved of their tension with no change in depersonalization. One patient recovered. He was a case of recent onset with marked obsessional and anxiety features. The results on the whole are poor.

Benzedrine and epanutin.—39 cases had a course of treatment with benzedrine 10 to 20 mg. daily. 27 showed no change. 10 cases were improved, generally slightly and only in their affect; one was much improved, but there was a probability that epilepsy complicated this illness, and another case showed improvement in derealization but not in depersonalization. Epanutin in increasing doses was tried with 23 patients, 18 without effect and 5 showed slight improvement. An epileptic patient had her fits controlled by benzedrine and epanutin, but she had a sudden onset of depersonalization when under treatment.

Vasodilators.—These had little or no effect. 13 cases were treated with 50 to 100 mg. t.d.s. of nicotinic acid for weeks without effect. Intravenous injections of 10 c.c. Afenil (CaCl₂-urea) were given daily to 7 patients for a fortnight. There was a slight relief of anxiety in 2 cases, and no change in the remainder.

TABLE IV.—RESPONSE TO TREATMENT.

	Total cases	Results			
		Recovered	Improved	No change	Worse
E.C.T. ...	39	2	4	23	10
Contin. narcosis ...	15	1	0	10	4
Benzedrine ...	39	0	2	37	0
Epanutin ...	23	0	5	18	0
Nicotinic acid ...	13	0	0	13	0
CaCl ₂ urea ...	7	0	0	7	0
Insulin comas ...	6	0	0	6	0
Leucotomy ...	1	1	0	0	0
Ether abreaction ...	14	4	7	3	0

Ether abreaction.—It occurred to Dr. William Sargant and myself [45] that abreaction under ether as a means of excitation might be attempted in the group.

unreality feelings appear worse, it is possible that the depression in its intense form has masked the depersonalization to some extent. Occasionally unreality feelings follow E.C.T. Janet [49] suggested many years ago that in the treatment of depersonalization, excitation is required to raise what he regarded as the lowered degree of consciousness. It is therefore interesting to point out the few successful results with extreme psychological stimulation under ether. This has only been done in a few cases and it appears necessary for a good result to have a lively affect and anxiety. The apathetic, dull or depressed patient responds with the utmost difficulty or not at all.

As Mayer-Gross pointed out, in discussing the mechanism of depersonalization, numerous theories advanced in the past are based on selected facts, and none satisfactorily include all facts. Thus, the following have all been invoked as causes of depersonalization: a "sinking in" of consciousness, a disturbance in temporal-spatial experience, an experience of the loss of volition. Or again a defence against reality, a shift in libido, or an investment of numerous phantom figures with insufficient ego libido in childhood. Finally disturbances at the neuro-physiological level, or disturbance of consciousness at its highest functional level, due to faulty integration and a generalized cerebral cortical dysfunction.

We know the following definite facts about the condition which may throw some light on its mechanism or aetiology.

The positive findings are:

The onset is practically always sudden.

Most typically the onset occurs in adolescence or early maturity.

It occurs as a symptom in a very wide range of psychiatric disorders.

It can occur in normal people as a fleeting experience, for example in fatigue, after anaesthetics, and experimentally during mescaline intoxication.

It is a reversible condition, cases can recover completely and spontaneously.

There is a significant relationship to migraine and to obsessional traits in our cases.

The onset is significantly related to relaxation following intense or prolonged stimulation, psychological or physical.

The condition may be relieved by stimulation.

The symptom can be experienced in any psychological field whether cognitive, affective or conative.

There is a distinct tendency for the symptom to occur in the more intelligent individual.

There is also a tendency for the disturbance to occur in emotionally immature subjects.

There is a high incidence of unsatisfactory parental-child relationship.

There is a higher incidence of non-specific mild abnormality in the E.E.G.s of this group than in any other groups except deteriorated cases.

The negative findings are:

It is not a disorder of visual perception.

It cannot be accounted for in neurological terms by any known focal lesion.

There is no specific relationship with anatomical disease of the brain.

There is a relative absence of olfactory, gustatory, or auditory derealization.

It is extremely rare in children.

It is practically never found in paranoia.

Since the experience can occur in almost anyone under certain conditions, just as a convulsion can, a preformed functional pattern must be present. In those instances where the experience occurs as a significant symptom, there is evidence of a constellation of constitutional deviations. These include obsessional personality, migraine, mild non-specific cerebral dysrhythmia, a specific age of onset, and relative intellectual superiority. Psychologically the patients show themselves as sensitive to the stresses of the child-parent relationship, emotionally immature and introverted. In such individuals, the symptom has a sudden onset, is curiously related to the relaxation following stress, and tends to respond to stimulation of various types. The mechanism of symptom-formation cannot be adequately considered in either physiological or psychological terms alone, nor can any single theory related to partial function be accepted.

become active, regained former interests and affection towards the family and no longer complains of depersonalization. Recently two further long-standing and intractable cases of depersonalization have shown marked benefit after leucotomy operation. The response to leucotomy has been promising but very few cases have so far been done and the response needs further assessment.

DISCUSSION

Our aim in this paper is to make a contribution towards the clinical, diagnostic, and prognostic features of depersonalization, the effects of treatment, and to the discussion of the mechanism involved in the production of this syndrome. One of our difficulties has been the description of what we mean by depersonalization. Since the mechanism is not known, the definition can only be descriptive. Short definitions can only be insufficient, and a complete one would include aspects to which attention has been drawn by many different workers. However, the experience is distressing and seems to be essentially one of unreality; the world feels unreal; the subject feels he is unreal, totally or partially; the symptom never seems to have a delusional quality in the type of case discussed in this paper. The patients have insight. They do not say "I am unreal" but "I feel I am not real, although I know I am." When they speak of a change in their personality, they seem always to refer to a sense of loss. The state bears no resemblance to the personality changes after concussion or encephalitis. The condition can occur in the early stages of all neurosis and psychosis and in some organic conditions but, as Haug [47] pointed out, it is practically absent in paranoia. It is rare in children and senile states. The form of the illness, such as depression or schizophrenia, will determine the quality of the experiences, for example, hallucinations based on depersonalization. Later in a progressive psychosis the symptom is lost, for instance it is lost in the stage of deterioration in schizophrenia. The question thus arises whether depersonalization depends on an intact affect. But it appears that there is a group defined by this paper and with which this paper deals, in which depersonalization exists almost alone and is a clinical entity. This has been called the depersonalization syndrome. Is this condition dependent on an unknown pathophysiological process? and, in this group, is the depersonalization related specifically to such process, or is the pattern determined by genetic or constitutional factors? If depersonalization is dependent on an abnormal brain state it is clear that this group constitutes the obvious material for investigation.

Clinically, the condition is commoner than is generally believed. Depersonalization is the fundamental experience and when it occurs as the predominant and presenting symptom, it has an obsessional quality. A sudden onset is often not described but is vividly remembered if recalled. There is a tendency for the patient to refer to the sudden onset as a "collapse" without further elaboration. Usually severe anxiety and fears follow it for some time, hence the frequent complaints of difficulty in breathing, sinking feeling in the stomach and so on. Depersonalization may easily be missed. Difficulties in diagnosis arise when the symptom causes marked anxiety and depression. The difficulty in describing the symptom, the perplexity to which it gives rise, and the fear of being regarded as insane, result in one or other somatic symptoms being presented, such as giddiness, pains in the head, faints, or fatigue. We have seen patients who have attended hospital for some time regarded as suffering from obsessional neurosis with anxiety in which depersonalization has passed unnoticed. Palmer [48], in discussing acute anxiety attacks in the obsessional group, says "the emphasis is laid on the psychic components, especially the unreality, of the anxiety attack" and that "a sense of unreality which may show itself as depersonalization or derealization, or both, may follow or replace, or constitute the most prominent symptom of the attack following the intense fear". We are stressing the depersonalization, and suggest that it may precede the anxiety. In some obsessional neurotics unreality feelings come and go. Occasionally apparent recurrent attacks of depersonalization prove to be intensifications of the symptom which has persisted throughout in a less intense form and has been accepted by the patient. What might be called primary idiopathic depersonalization starts suddenly in adolescence and may last many years. Generally those cases in our group which have lasted many years with little affective disturbance are those which have begun in adolescence. Clinically, it is found that the more primary the depersonalization, the more unvarying and unyielding it is. One of the reasons the condition is found comparatively frequently in an out-patient department is that the disability accompanying the symptom is mild though persistent. It is important to recognize the presence of depersonalization because of its prognostic significance and its resistance to treatment.

The response to treatment has already been fully discussed. It is largely of a negative character. In those cases in which convulsion therapy relieves the depression but the

unreality feelings appear worse, it is possible that the depression in its intense form has masked the depersonalization to some extent. Occasionally unreality feelings follow E.C.T. Janet [49] suggested many years ago that in the treatment of depersonalization, excitation is required to raise what he regarded as the lowered degree of consciousness. It is therefore interesting to point out the few successful results with extreme psychological stimulation under ether. This has only been done in a few cases and it appears necessary for a good result to have a lively affect and anxiety. The apathetic, dull or depressed patient responds with the utmost difficulty or not at all.

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Dr. W. Mayer-Gross: Dr. Shorvon's interesting clinical study of depersonalization is based on a larger number of patients than any one observer has collected before. Nevertheless, I doubt if his material covers the whole range of clinical pictures in which depersonalization occurs as the leading symptom. While obsessional personalities are preponderant among his cases, he apparently included only a few subjects of cyclothymic temperament. In the latter the symptom is frequent, in fact one-third of my own patients were of this type. It seems debatable if the excess of obsessional does not account for Dr. Shorvon's findings of unsatisfactory child-parent relationship, and also for some of his results in the Rorschach test. The onset of depersonalization in a state of relaxation after exertion is in good accord with its occurrence in normal fatigue and exhaustion. Relief of the symptom through excitation and mental effort corresponds to the relief of other psychoneurotic symptoms like stammering and phobias in situations of excitement. The results of experimental approach applied for the first time in such patients were disappointing, but not conclusive. Less conventional experimental methods should be tried and may have different results, especially as the abnormal brain potentials seem to point at a distinctive functional disturbance. Finally, I find it difficult to agree with Dr. Shorvon's suggestion of "Primary Idiopathic Depersonalization" as a disease entity, considering the present provisional state of psychiatric classification. We already know of a number of constitutional and incidental factors as well as illnesses on which the presence of the symptom depends. The few cases in which none of these factors is found hardly justify the claim for a special class of disease.

Section of Comparative Medicine

President—W. A. POOL, M.R.C.V.S.

[June 19, 1946]

Penicillin Concentration in the Blood and Milk of Bovines

By GEORGE SLAVIN

THE use of penicillin in animal diseases will presumably follow similar lines to those in man but with the compounds at present available and the fact that animals are rarely given hospital treatment, its scope will be more restricted.

GENERAL TREATMENT

We have tried this in cows suffering from low-grade mastitis which had resisted penicillin treatment by direct injection into the udder. The first cow was excreting a Group C streptococcus and was given 128,000 units of sodium penicillin i.m. every three hours for twenty-four hours. With the methods available for the estimation of penicillin in milk none could be detected but the infection suddenly disappeared. The highest blood level reached was approximately $\frac{1}{4}$ unit per c.c. A second cow, which was excreting *Str. agalactiae*, *Str. uberis* and *C. pyogenes*, was given 114,000 units in the same way for the same period, but the infection persisted. The highest blood level reached was again about $\frac{1}{4}$ unit per c.c. This second cow might have responded to a longer course of injections.

The blood levels in these cows seemed to follow the same lines as has been found in man. To get a complete picture a normal cow was given a single injection of 200,000 units of calcium penicillin i.m. and blood samples were collected every five minutes up to 40 minutes, then at 50 minutes, 60 minutes, 133 minutes, 170 minutes, 210 minutes and 240 minutes. The blood levels are shown in fig. 1. The highest level was at 5 minutes with a steady fall until 20 minutes; from then until 60 minutes there was some variation and the level then resumed its steady fall until penicillin could no longer be detected

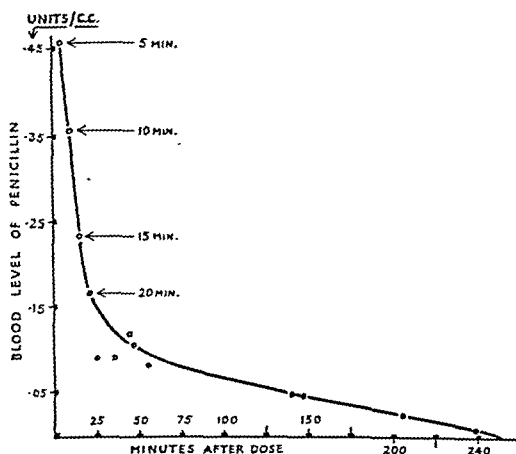


FIG. 1.—Blood levels of penicillin after a single injection of 200,000 units of calcium penicillin intramuscularly.

at 240 minutes. The two points at 133 and 138 minutes were inserted as a test of the accuracy of the method of estimation.

As it is obviously impossible to use three-hourly injections in practice, the use of oily suspensions was investigated. It was found that 1 mega unit of penicillin in 4% beeswax-arachis oil every twelve hours gave satisfactory blood levels, showing that about ten times the dose given in water was required in order to produce the same blood level. These oily suspensions were injected subcutaneously, mostly at the side of the neck, in order to avoid muscle lesions which might lead to condemnation of part of the carcass. The calcium penicillin used was of low potency and the minimum volume of the injection was about 10 c.c. The inoculum caused a considerable reaction which will, we believe, disappear in time.

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Dr. W. Mayer-Gross: Dr. Shorvon's interesting clinical study of depersonalization is based on a larger number of patients than any one observer has collected before. Nevertheless, I doubt if his material covers the whole range of clinical pictures in which depersonalization occurs as the leading symptom. While obsessional personalities are preponderant among his cases, he apparently included only a few subjects of cyclothymic temperament. In the latter the symptom is frequent, in fact one-third of my own patients were of this type. It seems debatable if the excess of obsessionals does not account for Dr. Shorvon's findings of unsatisfactory child-parent relationship, and also for some of his results in the Rorschach test. The onset of depersonalization in a state of relaxation after exertion is in good accord with its occurrence in normal fatigue and exhaustion. Relief of the symptom through excitation and mental effort corresponds to the relief of other psychoneurotic symptoms like stammering and phobias in situations of excitement. The results of experimental approach applied for the first time in such patients were disappointing, but not conclusive. Less conventional experimental methods should be tried and may have different results, especially as the abnormal brain potentials seem to point at a distinctive functional disturbance. Finally, I find it difficult to agree with Dr. Shorvon's suggestion of "Primary Idiopathic Depersonalization" as a disease entity, considering the present provisional state of psychiatric classification. We already know of a number of constitutional and incidental factors as well as illnesses on which the presence of the symptom depends. The few cases in which none of these factors is found hardly justify the claim for a special class of disease.

Milk.—Milks were titrated against a standard penicillin on a large double layer blood agar plate using a Group A streptococcus as test organism. The plate takes 48 tests in holes punched through the upper layer. The method is sensitive down to 0.07 unit and with care it will detect as little as 0.031 unit. The plate is easy to set up and a large number of estimations can be done quickly.

Lady Florey: Penicillin concentrations in serum after a single intramuscular injection in the cow as shown by Dr. Slavin follow much the same curve as has been found in man. A sharp initial fall is followed by a flattening indicating probably that there is an optimum concentration in the blood-stream below which excretion is minimal. Relatively large doses producing initial high blood concentrations do not therefore produce correspondingly long periods of inhibition.

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Mr. K. D. Downham stated that he had treated 50 cows suffering from streptococcal mastitis and that 75% of these animals had been freed from infection, as shown by four subsequent bacteriological examinations of milk samples. He had had no success in the treatment of mastitis due to *C. pyogenes* in dry cows. He described a cow which had suffered from mastitis due to infection with *Str. agalactiae*, whose milk had contained these organisms for eighteen months, and which failed to respond to routine udder infusion with penicillin, but was successfully treated when penicillin was administered in a dosage of 30,000 units in each quarter for two successive days on several occasions with two days' interval after each two days' treatment. This method of intermittent treatment appeared to be of value in the treatment of cows which failed to respond to the routine method of infusion. The cow's milk was found to be free from *Str. agalactiae* organisms when examined on four occasions after this method of treatment.

An Outbreak of Industrial Fluorosis in Cattle

By H. H. GREEN, D.Sc.

It may be recalled that in the "Discussion on Fluorosis in Man and Animals" by this Section in February 1941¹ the occurrence of severe fluorosis in cattle was described on farms in the vicinity of brickworks in Bedfordshire. The purpose of the present communication is to report a similar occurrence associated with the calcining of ironstone in Lincolnshire. In this process the raw ironstone is mixed with about 7% of its weight of coal and ignited in the open, fresh layers being added to form a smouldering mound, the complete calcining of which occupies several weeks. The weight of the ironstone is so reduced for transport, and the ore rendered sufficiently porous for direct reduction in blast furnaces at distant smelting centres.

During the calcining process smoke drifts on to neighbouring farms, and on the nearest of these an obscure disease of cattle was reported by G. A. Moore, M.R.C.V.S. Samples of urine from affected cases, analysed at Weybridge, at once established a diagnosis by revealing 26 to 69 parts per million of fluorine. Analyses of materials collected during a visit to the area showed 1,200 p.p.m. fluorine in the ironstone itself and 100 to 180 p.p.m. in the various types of coal used. The calcined ore contained only 300 p.p.m., thus revealing a loss of three-quarters of the original fluorine or about four-fifths if loss of weight be allowed for. Imitation of the calcining process in the laboratory showed approximately 90% loss of fluorine at controlled muffle temperature of 850° C., but negligible loss at 600° C. It seems probable that the fluorine comes off as silicon fluoride which, reacting with atmospheric moisture and ammonia from the coal, condenses on the smoke particles as ammonium fluoride and silicofluoride and drifts on to the pastures. Samples of water from the affected farm showed only 0.5 p.p.m. fluorine but grass samples within a few hundred yards of the burning mounds showed over 2,000 p.p.m. on the dry matter. A straw stack about half a mile away showed 490 p.p.m. on the exterior and 70 p.p.m. in the interior. The danger zone has not yet been mapped out but it is not likely to exceed a radius of 2 miles.

¹Proc. R. Soc. Med., 34, 391.

LOCAL TREATMENT

Local treatment has been tested on a fairly large scale during the last year but has been confined entirely to mastitis. Considerable success has followed its use in streptococcal mastitis, somewhat less success in staphylococcal mastitis, and so far it has failed in *C. pyogenes* infection although this organism is sensitive to penicillin.

A solution of penicillin in about 50 c.c. of water is injected through the teat canal. Various doses have been tried but the most practicable and successful method is two injections of 100,000 units at twenty-four-hour intervals.

An extensive series of tests was made to follow the fate of the injected penicillin and the concentration in the udder secretion is seen in Tables I to IV.

TABLE I.—RESULTS IN 5 COWS GIVEN 20,000 UNITS PER QUARTER 24 HOURS PREVIOUSLY.

Cow	Qtr.	Yield in lb.	pH	Units of penicillin per c.c.
587	LF	0.75	7.33	0.36
	LH	3.75	6.88	1.0
	RF	0.5	7.20	0.4
	RH	4.25	6.83	0.8
720	LF	0.75	6.80	0.3
	LH	0.5	6.80	0
	RF	1.0	6.00	1.8
	RH	1.5	6.82	0.3
429	LF	Too small	7.45	10.0
	LH	small	7.31	1.0
	RF	to weigh	7.42	4.5
	RH		7.58	0.8
397	LF	1.25	6.78	0
	LH	2.75	6.80	0
	RF	0.75	7.08	0
	RH	2.5	6.97	0
647	LF	1.0	6.94	0
	LH	2.0	6.74	0
	RF	1.25	6.80	0
	RH	0.25	6.73	0

TABLE II.—CONCENTRATION IN COWS 24 HOURS AFTER INJECTION OF 100,000 UNITS.

Cow	Qtr.	Yield in lb.	pH	Units per c.c.
478	LF	1.75	6.85	3.1
	LH	—	7.20	350
	RF	0.5	7.28	50
	RH	4.5	6.72	3.5
644	LF	0.75	6.8	0
	LH	1.75	6.82	0
	RF	2.0	6.68	1.6
	RH	0.75	7.08	0.125
583	LF	Too small	—	72
	LH	small	7.48	72
	RF	to weigh	7.47	350
	RH		7.33	100
568	LF	0.5	7.12	2.5
	LH	0.75	7.27	0.5
	RF	0.75	7.19	3.5
	RH	0.75	7.30	0.125
458	LF	Too small	7.38	400
	LH	small	7.45	100
	RF	to weigh	7.30	72
	RH		7.40	100

TABLE III.—THE SAME COWS 96 HOURS AFTER A SECOND INJECTION OF 100,000 UNITS.

Cow	Qtr.	Condition of milk	pH	Units per c.c.
478	LF	Normal	6.7	0
	LH	Pus	—	0
	RF	Normal	7.86	0
	RH	Normal	6.67	0
644	LF	Normal	7.33	0
	LH		7.24	0
	RF		6.88	0
	RH		7.6	0
583	LF	Pus	7.42	1.5
	LH	Clots	7.38	0.08
	RF	No milk	—	0
	RH	Pus	7.70	0
568	LF	Normal	7.38	0
	LH		—	0
	RF		7.10	0
	RH		7.41	0
458	LF	Pus	—	0.4
	LH	all	7.47	1.0
	RF	qtrs.	—	0.62
	RH		7.58	1.4

TABLE IV.—PENICILLIN CONCENTRATIONS IN THE UDDER OF 4 COWS UP TO 144 HOURS AFTER A SECOND INJECTION OF 100,000 UNITS.

Cow	Qtr.	24	24	48	72	96	120	144
91	LF	20	50	5.6	0.62	0.07	0	—
	LH	37	50	10	2.5	1.25	0.47	0
	RF	44	> 150	25	20	5	3.5	1.25
	RH	50	> 200	15	2.5	0.31	+	—
116	LF	28	50	3.3	0	—	—	—
	LH	37	150	5	0	—	—	—
	RF	100	> 200	10	0	—	—	—
	RH	89	> 300	20	2.33	0.17	0	—
125	LF	89	> 200	25	10	0.47	0	—
	LH	100	> 150	12.5	2.5	0.31	0	—
	RF	89	> 200	33	2.3	0.27	0	—
	RH	79	500	100	20	1.5	0.17	0
203	LF	2.2	1.0	0	—	—	—	—
	LH	0.71	0.75	0	—	—	—	—
	RF	1.5	6.2	0	—	—	—	—
	RH	2.5	6.2	0.15	0	—	—	—

+ = less than 0.07 unit.
 — = no sample.

METHODS OF ESTIMATION

Blood.—This was carried out mostly by the slide cell method using either the "Oxford" staphylococcus or a Group A streptococcus, the latter being a very sensitive organism. Unfortunately slide cells are tedious to prepare. We have also tried capillary tubes but the method is less sensitive and we have not had the same degree of success as with slide cells. In both methods the margin of error is large. Dilution methods in broth using the "Oxford" staphylococcus are less laborious and we believe them to be considerably more accurate. The degree of inhibition is read against a standard curve. We have been able to detect about 1/1000 of a unit by this method. To avoid the necessity for large volumes of blood the tests are read in tubes similar to those used for standardizing vaccines against the Brown opacity scale. We prepared our own tubes because the commercially produced ones showed large differences in the glass.

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Cattle on the nearest farm were stunted and lame and the owner described some of the earlier cases as having to be destroyed after "crawling on their knees". Two cases have been purchased for post-mortem study by F. Blakemore at Cambridge and will doubtless show lesions similar to those described in 1941.

The human family on the same farm is a large one and urine samples of 9 people showed from 1.3 p.p.m. to 4.2 p.p.m. fluorine, averaging less than one-tenth that of the cattle urines but nevertheless being above normal and far above the value in the drinking water. Surface contamination of green vegetables is suggested as the source. Dr. Dagmar Wilson has been asked to consult with the local M.O.H. with regard to clinical symptoms in the children.

Dr. Dagmar Wilson: Our knowledge of human fluorosis has been considerably extended since fluorine was the subject of discussion by this Section in 1941. Fluorine is now generally recognized as an important trace element in human nutrition which exerts influence at non-toxic as well as at toxic levels.

The incidence of fluorotic lesions probably bears a definite relation to the economic and nutritional status of a community. A small amount of fluorine—under 1.0 p.p.m.—is present in many British water supplies and a lowered incidence of dental caries is found amongst people who have used a drinking water containing 0.5 to 1.0 p.p.m. fluorine for at least the first eight years of life. In the United States fluorination of water supplies is being considered for the partial control of dental caries. Human balance experiments show a close correlation between fluorine in the drinking water and in urine, and the elimination of fluorine is practically complete when the quantity absorbed does not exceed 5 mg. daily.

In human toxic fluorosis acute generalized and local effects are usually accidental. Chronic poisoning in man occurs in two ways, as chronic endemic fluorosis and as an occupational disease. Bone abnormalities and systemic illness, of which gastric derangement is an early sign, may occur when fluorine tolerance levels are exceeded.

Fluorides are being increasingly used in industry and large amounts of fluorine are associated with recent industrial development in this country. Methods for the control of the fluorine evolved are known and are not difficult of application, but the fluorine hazards for factory workers, for their families living near-by, and for other people resident or employed in the neighbourhood, as well as for the animal population, are not sufficiently appreciated.

Dr. Margaret M. Murray: In 1937 when Roholm's book "Fluorine Intoxication" was published and reviewed, my attempts to interest appropriate persons in the possibility of a fluorine hazard to human beings in Great Britain, particularly in the Scottish Highlands, failed. Since then we know of three outbreaks of fluorosis in farm animals and it is significant that in each case it was the effects on grazing animals which brought to light the existence of the fluorine hazard; consideration of the effects on human beings has in each case been secondary.

We owe it to Dr. H. H. Green and his colleagues that the cause of the outbreak in the Marston Valley was discovered and the plans for elimination of the danger were successfully worked out.

At Fort William it was because sheep in the vicinity of the aluminium works did not thrive that an inquiry was made into the question of a hazard to human beings. Examining school children at Inverlochy, which has only 0.2 p.p.m. fluorine in the drinking water and which is situated in the direction of the prevailing wind carrying the fumes from the aluminium works, Dr. Wilson and I found the white mottling of dental fluorosis present even in the temporary teeth. We were, and still are, at a loss to explain what was the source of the fluorine which caused this mottling, particularly of temporary teeth.

Dr. Green's investigations show the fundamental importance and usefulness of the determination of fluorine in urine in the study of fluorine intoxication. These outbreaks of fluorosis in farm animals have also shown that not all animals are similarly affected by the ingestion of toxic amounts of fluorine. In cows the long bones are severely affected, while in the sheep at Fort William, investigated by Professor Boddie of the Royal Dick Veterinary College, Edinburgh, it was the jaw bones which were grossly abnormal and because of this the animals could not obtain food. This is the condition seen in the sheep, goats, camels and horses of the "darmous" region of Morocco. In man it is usually the vertebral column which is first affected and this effect may not be detectable until there has been a long period of exposure. Therefore, in the absence of positive X-ray findings, the only means of testing for the ingestion of fluorine at levels which will ultimately cause these bone changes, is by the determination of fluorine in the urine.

REFERENCE

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The Chick-Embryo in Chemotherapeutic Research. [Summary]

By JOHN FRANCIS, B.Sc., M.R.C.V.S.

OCSTON (1881) was probably the first to cultivate bacteria in the incubating egg, but with the development of satisfactory culture media his work was forgotten. Goodpasture (1938) reviewed other early work with the chick-embryo and Landauer (1941) published an extensive monograph on the factors which influence the hatchability of eggs. Buddingh and Polk (1939a and b) found that by using embryos of suitable ages and inoculating meningococci by various routes they could produce lesions of septicaemia, sinusitis, pneumonia and meningitis, similar to those found in the natural disease; in addition they showed that immune serum had a protective effect. Following this work a considerable number

of chemotherapeutic experiments have been carried out (Green, 1944; Griefff *et al.*, 1944; Koprowski, 1944; Weil, 1941) but no one has made a systematic study to show how the chick-embryo may be used to demonstrate various types of therapeutic activity. When we began our work with the chick-embryo in 1942 (Francis, 1944) we were particularly interested in bovine mastitis. Because of the great variation in the severity and course of mastitis, associated with *Str. agalactiae*, it is almost impossible to compare the value of a large series of drugs against the natural disease. At that time no one had established an easily reproducible disease in mice with *Str. agalactiae* and we hoped that the chick-embryo would prove a suitable experimental "animal" for selecting drugs useful in the treatment of mastitis. The chick-embryo has been successfully used for this purpose and at the same time we have made observations of more general interest showing how various types of therapeutic activity may be demonstrated.

EXPERIMENTAL

Both the infecting organism and the drug can be inoculated by several different routes and in most of our work we have inoculated bacteria on to the chorio-allantois, and have inoculated drugs by a variety of routes one hour later. It can be seen from the accompanying diagram (fig. 1) that if the drug, as well as the bacteria, is inoculated on to the

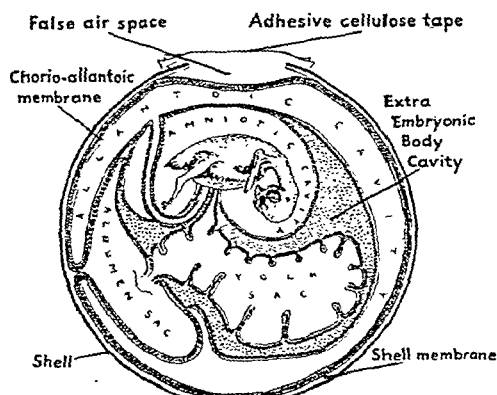


FIG. 1.—The relative position of the embryo and its membranes after twelve days' incubation (after Lilly).

chorio-allantois, treatment will resemble local application to a wound or into an infected peritoneum. Inoculation of the drug into the allantois may be compared with intravenous or intramuscular therapy and inoculation into the yolk sac bears some resemblance to oral dosing.

Although we have used *Str. agalactiae* most extensively, similar results would undoubtedly have been obtained with Group A streptococci. We have shown that 0.5 to 1 mg. of proflavine has a marked therapeutic effect when applied on to the chorio-allantois but little or none when inoculated into the allantois or yolk sac. We found the sulphonamide drugs equally potent when they were applied directly on to the chorio-allantois, or inoculated into the allantois or yolk sac. Penicillin was, however, considerably more active when applied on to the chorio-allantois than when given by the other two routes.

The Relative Potencies of Various Drugs against *Str. agalactiae*

We have compared the potencies of 4.4' diamino-diphenyl sulphone (sulphone) and various sulphonamides in a large series of experiments. The results have been statistically analysed and are shown in Table I. It will be seen that sulphapyridine and sulpha-

TABLE I.—THE RELATIVE POTENCIES OF VARIOUS DRUGS AGAINST *STR. AGALACTIAE*.

	Chick-embryo	Intrinsic potency in mouse (for comparison)	<i>In vitro</i> in milk
Sulphanilamide	1	1	1
Sulphapyridine	1.25	1.25	
Sulphadiazine	1.30	2.0	
Sulphamezathine	1.84	1.22	
Sulphathiazole	2.33	1.8	
Sulphone	3.15	3.0	4.8

diazine are only slightly more active than sulphanilamide, but sulphone is just over three times as active; sulphamezathine and sulphathiazole occupy an intermediate position. We have found that similar doses of the various sulphonamides produce similar blood

Cattle on the nearest farm were stunted and lame and the owner described some of the earlier cases as having to be destroyed after "crawling on their knees". Two cases have been purchased for post-mortem study by F. Blakmore at Cambridge and will doubtless show lesions similar to those described in 1941.

The human family on the same farm is a large one and urine samples of 9 people showed from 1.3 p.p.m. to 4.2 p.p.m. fluorine, averaging less than one-tenth that of the cattle urines but nevertheless being above normal and far above the value in the drinking water. Surface contamination of green vegetables is suggested as the source. Dr. Dagmar Wilson has been asked to consult with the local M.O.H. with regard to clinical symptoms in the children.

Dr. Dagmar Wilson: Our knowledge of human fluorosis has been considerably extended since fluorine was the subject of discussion by this Section in 1941. Fluorine is now generally recognized as an important trace element in human nutrition which exerts influence at non-toxic as well as at toxic levels.

The incidence of fluorotic lesions probably bears a definite relation to the economic and nutritional status of a community. A small amount of fluorine—under 1.0 p.p.m.—is present in many British water supplies and a lowered incidence of dental caries is found amongst people who have used a drinking water containing 0.5 to 1.0 p.p.m. fluorine for at least the first eight years of life. In the United States fluorination of water supplies is being considered for the partial control of dental caries. Human balance experiments show a close correlation between fluorine in the drinking water and in urine, and the elimination of fluorine is practically complete when the quantity absorbed does not exceed 5 mg. daily.

In human toxic fluorosis acute generalized and local effects are usually accidental. Chronic poisoning in man occurs in two ways, as chronic endemic fluorosis and as an occupational disease. Bone abnormalities and systemic illness, of which gastric derangement is an early sign, may occur when fluorine tolerance levels are exceeded.

Fluorides are being increasingly used in industry and large amounts of fluorine are associated with recent industrial development in this country. Methods for the control of the fluorine evolved are known and are not difficult of application, but the fluorine hazards for factory workers, for their families living near-by, and for other people resident or employed in the neighbourhood, as well as for the animal population, are not sufficiently appreciated.

Dr. Margaret M. Murray: In 1937 when Roholm's book "Fluorine Intoxication" was published and reviewed, my attempts to interest appropriate persons in the possibility of a fluorine hazard to human beings in Great Britain, particularly in the Scottish Highlands, failed. Since then we know of three outbreaks of fluorosis in farm animals and it is significant that in each case it was the effects on grazing animals which brought to light the existence of the fluorine hazard; consideration of the effects on human beings has in each case been secondary.

We owe it to Dr. H. H. Green and his colleagues that the cause of the outbreak in the Marston Valley was discovered and the plans for elimination of the danger were successfully worked out.

At Fort William it was because sheep in the vicinity of the aluminium works did not thrive that an inquiry was made into the question of a hazard to human beings. Examining school children at Inverlochy, which has only 0.2 p.p.m. fluorine in the drinking water and which is situated in the direction of the prevailing wind carrying the fumes from the aluminium works, Dr. Wilson and I found the white mottling of dental fluorosis present even in the temporary teeth. We were, and still are, at a loss to explain what was the source of the fluorine which caused this mottling, particularly of temporary teeth.

Dr. Green's investigations show the fundamental importance and usefulness of the determination of fluorine in urine in the study of fluorine intoxication. These outbreaks of fluorosis in farm animals have also shown that not all animals are similarly affected by the ingestion of toxic amounts of fluorine. In cows the long bones are severely affected, while in the sheep at Fort William, investigated by Professor Boddie of the Royal Dick Veterinary College, Edinburgh, it was the jaw bones which were grossly abnormal and because of this the animals could not obtain food. This is the condition seen in the sheep, goats, camels and horses of the "darmous" region of Morocco. In man it is usually the vertebral column which is first affected and this effect may not be detectable until there has been a long period of exposure. Therefore, in the absence of positive X-ray findings, the only means of testing for the ingestion of fluorine at levels which will ultimately cause these bone changes, is by the determination of fluorine in the urine.

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The Chick-Embryo in Chemotherapeutic Research. [Summary]

By JOHN FRANCIS, B.Sc., M.R.C.V.S.

OGSTON (1881) was probably the first to cultivate bacteria in the incubating egg, but with the development of satisfactory culture media his work was forgotten. Goodpasture (1938) reviewed other early work with the chick-embryo and Landauer (1941) published an extensive monograph on the factors which influence the hatchability of eggs. Buddingh and Polk (1939a and b) found that by using embryos of suitable ages and inoculating meningococci by various routes they could produce lesions of septicaemia, sinusitis, pneumonia and meningitis, similar to those found in the natural disease; in addition they showed that immune serum had a protective effect. Following this work a considerable number

in mice with *Str. agalactiae*. The relative potencies of the various drugs against this infection are shown in Table I, after allowance has been made for the different blood-levels produced in the mouse. Again it will be seen that sulphone was the most potent drug but sulphadiazine was relatively more potent than in the chick-embryo.

(3) The potencies of some solubilized derivatives were similar to those of the parent compound but sulphanilamide L.S.F. was inactive in our experiments. The activity of various antiseptics was also compared.

(4) The sulphonamides exerted no effect on the multiplication of *C. pyogenes* in the chick-embryo. Penicillin inhibited multiplication of *C. pyogenes* but we have not been impressed with the therapeutic activity of penicillin in the chick-embryo, and its efficiency in preventing death of embryos inoculated with unfiltered sputum (Rose *et al.*, 1945) may be due to the fact that these workers mixed the sputum with the penicillin before inoculation, thus allowing it to exert a direct bactericidal effect.

(5) In common with some other workers we have found that the results obtained in the chick-embryo are rather less consistent than those obtained in the mouse, but certain types of tests can be carried out which cannot be performed in the mouse, and the chick-embryo is susceptible to a number of infections to which laboratory animals are resistant.

The detailed results on which this paper is based will be submitted for publication elsewhere.

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Leishmaniasis in Greece

By B. MALAMOS, M.D., D.T.M.

(From the London School of Hygiene and Tropical Medicine, Department of Parasitology)

HUMAN visceral leishmaniasis, canine leishmaniasis and oriental sore are endemic in Greece and, curiously enough, co-exist in some districts.

New foci of kala azar or human visceral leishmaniasis are constantly being discovered. The widest endemic focus seems to be in Messinia; cases also occur in the Peloponnese in the regions of Argos, Nauplia, Patras, Poros, and the islands of Spetsai and Hydra. The disease is also found in Athens, Piraeus, Salamis, the Ionian Islands, Lamia, Thessaly, Macedonia, and, more especially, in Crete.

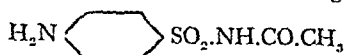
Kala azar is, in Greece, predominantly a children's disease, occurring mostly in children between 2 and 4 years of age. It is common to find two or more cases in the same house. The clinical picture is that well known for the Mediterranean type of the disease. The dark pigmentation of the skin, however, did not occur in all of our cases. It is strange that in some villages all the cases showed skin haemorrhages while in neighbouring ones not one with this hemorrhagic diathesis was encountered. For the diagnosis we prefer to demonstrate *L. donovani* by puncture of the spleen or the sternum, using for spleen puncture the Aravantinos syringe (fig. 1). Serological diagnostic methods are not employed to the same extent. For therapeutic purposes we use relatively higher doses of drugs than those used in Eastern Asia.

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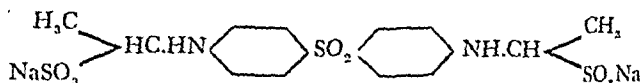
The sodium salts of the sulphonamides, except sulphacetamide, are too irritant for infusion into the udder, but there are a number of soluble derivatives available and we have compared their activity¹ against *Str. agalactiae* infection in a smaller series of experiments.

The following drugs were compared at doses of 5 to 10 mg.:

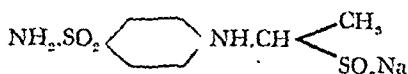
Sulphacetamide



The E.O.S.* derivative
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Sulphanilamide L.S.F. A solution of sulphanilamide lactoside, sodium formaldehydesulphoxylate.

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Free sulphanilamide exerted its usual therapeutic activity, but sulphacetamide was about four times less active. The activity of sulphanilamide as the E.O.S. derivative was about the same as that of the free drug, but the L.S.F. derivative had no therapeutic effect in these experiments. The E.O.S. derivative of sulphone again had about the same activity as the free compound. These differences are, no doubt, due to variations in the dissociation of the complex molecules and it appears that sulphanilamide L.S.F. hardly dissociates at all in the chick-embryo.

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In addition, we have found that the sulphonamides have little or no action against *C. pyogenes* infection in the chick-embryo, which confirms clinical observations, but penicillin does prevent multiplication of the organism. We have tested about one hundred speculative compounds against this infection, but so far we have not found one likely to be of any great therapeutic value.

During the course of the foregoing experiments we have, at times, had a considerable number of embryos die due to bacterial contamination by Gram-negative organisms. Sixteen strains have been isolated and all but two gave the following biochemical reactions:

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DISCUSSION AND SUMMARY

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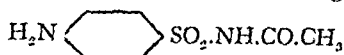
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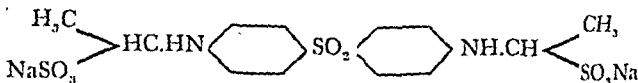
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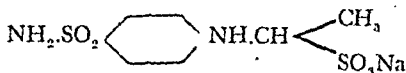
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Leishmaniasis in Greece

By B. MALAMOS, M.D., D.T.M.

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HUMAN visceral leishmaniasis, canine leishmaniasis and oriental sore are endemic in Greece and, curiously enough, co-exist in some districts.

New foci of *kala azar* or human visceral leishmaniasis are constantly being discovered. The widest endemic focus seems to be in Messinia; cases also occur in the Peloponnese in the regions of Argos, Nauplia, Patras, Poros, and the islands of Spetsai and Hydra. The disease is also found in Athens, Piraeus, Salamis, the Ionian Islands, Lamia, Thessaly, Macedonia, and, more especially, in Crete.

Kala azar is, in Greece, predominantly a children's disease, occurring mostly in children between 2 and 4 years of age. It is common to find two or more cases in the same house. The clinical picture is that well known for the Mediterranean type of the disease. The dark pigmentation of the skin, however, did not occur in all of our cases. It is strange that in some villages all the cases showed skin hæmorrhages while in neighbouring ones not one with this hæmorrhagic diathesis was encountered. For the diagnosis we prefer to demonstrate *L. donovani* by puncture of the spleen or the sternum, using for spleen puncture the Aravantos syringe (fig. 1). Serological diagnostic methods are not employed to the same extent. For therapeutic purposes we use relatively higher doses of drugs than those used in Eastern Asia.

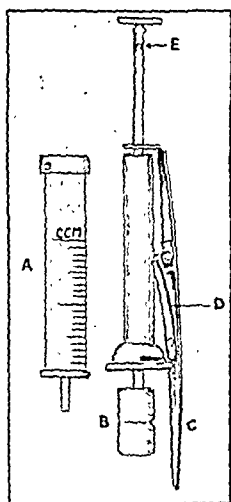


FIG. 1.—Aravantinos spleen puncture syringe. A, 2 c.c. record syringe. B, Piston. C, Metal leaf. D, Spring. E, Ring for insertion of metal leaf. The mechanism is as follows: On making the puncture the metal leaf is inserted in the ring. At the precise moment of puncturing the spleen pulp, the syringe is withdrawn and the metal leaf is pressed. The piston is automatically withdrawn and there is then enough pulp in the needle to make two or three slides.



FIG. 2.



FIG. 3.



FIG. 5.



FIG. 6.



FIG. 4.



FIG. 7.

Oriental sore occurs more particularly in Crete, in the districts of Canea, Rethymnon, Candia and also in Lakonia in the Peloponnese. Sporadic cases are found in various other districts of Greece, even in Athens. Outbreaks of oriental sore often take on an epidemic character.

This disease is common to all ages, affecting more particularly the uncovered parts of the body. The lower limbs are seldom affected in adults, but often in children. In some cases only one sore is found, in others a hundred or more can be counted. Many of the fresh sores are not ulcerated and have an acneiform appearance (fig. 2) and diagnosis is only possible by the detection of the parasite, *L. tropica*, in smears obtained from the peripheral regions of the sore (figs. 3 and 4). Various treatments are used for cure but none is absolutely effective. Usually local emetine injections are given, or treatment by mepacrine is used, and in Canea 10% powdered vegetable charcoal in concentrated sulphuric acid is often applied locally (figs. 5 and 6). This form of treatment is employed by the people themselves. In oriental sore regions various other skin diseases are often mistaken as being due to *L. tropica*.

Canine leishmaniasis.—This disease in Greece is very common and skin lesions are not rare in dogs. The infection is due only to the parasite of visceral leishmaniasis and never to *L. tropica*. Canine leishmaniasis is found in all regions in which we find human kala azar. It is very often said that in the same or neighbouring houses a canine case preceded a human infection. The clinical picture in dogs is characterized by emaciation, trichoptosis, eczema furfuraceum, ulceration of the skin and mucous membranes, diarrhetic motions, conjunctivitis and keratitis (fig. 7). Very characteristic are ulcerations at the base of the ear. In our mass examinations with M. Mayer in the Canea region we found 50% of the infected dogs with macroscopically normal appearance. The parasite is found in the internal organs, namely spleen, liver, bone-marrow and intestine. The skin, however, is the tissue which seems to contain the greatest number of parasites. We found *Leishmania*, also, in parts of the skin which macroscopically seemed to be normal.

Canine leishmaniasis is, in Greece, more common than human kala azar and it is the endemic form of *L. donovani* which, normally infecting dogs, attacks human beings. From the examination of dogs the following percentages were established of infected animals; in Athens, Cardamatis 8.15%, Lépine and Bilfinger 11 to 12%; in Piraeus, Cardamatis 7.5%; in Hydra, Lignos 16.6%; in Mani, Caminopetros 16%; and in Canea, Papantonakis 20.5%, Adler, Theodor and Witenberg 10%, M. Mayer and the writer 5.1%. In our mass examinations, out of 666 dogs examined in the Canea region all those infected came from the districts of the town and villages where human kala azar cases were to be found. Not a single dog from Splatzia, where oriental sore is endemic, was found to be infected.

It is obvious that if we want to be successful in preventing the spread of human kala azar, we must direct our campaign first towards the infected dog, the reservoir of the parasite. The best measures to be taken with this object in view were published by Papantonakis in the Greek *Official Gazette*, 1937, No. 79, vol. B.

The mode of transmission of leishmaniasis is important. That this transmission has now been proved to take place through the sandfly is due to the excellent work of Shortt (Director of Dept. of Parasitology, Lond. Sch. Hyg. Trop. Med.). *Phlebotomus perniciosus* is considered to be the vector of human and canine visceral leishmaniasis and our observations have proved that for Greece, *Phl. major* and not *Phl. perniciosus* must be considered as responsible for the transmission of this disease.

The main vector of oriental sore in Greece, on the other hand, is the species *Phl. sergenti* and only occasionally *Phl. papatasi*.

From this general and short survey of the vectors of leishmaniasis, it can be realized that the co-existence of the three forms of leishmaniasis can be explained and is most clearly exemplified in Canea (Crete).

Thus, oriental sore occurs principally in Splatzia, the old Turkish centre of the town. The streets there are very narrow with lack of vegetation. 53% of the collected sandflies were *Phl. sergenti* and 47% *Phl. papatasi*. None of the dogs examined was infected. In contrast to this, in the peripheral regions of the town where the houses are of the bungalow type with small gardens and some vegetation we find human and canine visceral leishmaniasis. 49% of the sandflies examined there were *Phl. major*, 45% *Phl. papatasi* and only 6% *Phl. sergenti*.

It is hoped that by the measures taken against infected dogs, as well as by recent improvements in insecticides we shall soon be able to eradicate these diseases.

A fuller account will appear in the *Tropical Diseases Bulletin*, for January 1947.

[July 31, 1946]

DISCUSSION ON DIGESTION IN THE RUMINANT. [Summarized].

A FILM was shown on "The Function of the Ruminant Stomach."

Dr. P. J. Du Toit introduced the film and the subsequent discussion.

He explained that for some years digestion in the ruminant has been investigated at the Onderstepoort Laboratory, South Africa, the work being in charge of Dr. J. I. Quinn, and that the film was made in order to illustrate some phases of the problems involved. Dr. Du Toit had brought the film over to Europe with him in the hope that it would prove to be of interest and stimulate the investigation of this little-known subject. It was not an account of the work done by the Staff at Onderstepoort, but was rather an account of some of the questions that require to be given consideration by those to whom the nutrition of cattle is important. He regretted that none of the Staff who had dealt with the subject were present to describe their work.

Dr. S. R. Elsden: Before we can consider the problem of ruminant digestion in detail we have to know what in fact is the chemical nature of the substances to be digested. Broadly speaking, the fundamental difference between the diet of herbivores, on the one hand, and that of omnivores and carnivores, on the other, is to be found in the carbohydrate fraction. The carbohydrate fraction of the herbivorous diet can be roughly divided into (a) cellulose, associated with a variable amount of lignin, depending on the nature of the diet; (b) hemicellulose and pentosans; (c) polysaccharides, e.g. starch and fructosan; (d) simple sugars such as glucose and sucrose. The first point I want to make is that we know very little of the chemistry of (a) and (b), particularly (b); and secondly, we know even less of the quantitative distribution of each of the four types in feeding stuffs. Here then is the first of the basic problems which must be tackled before a completed picture of ruminant digestion can be obtained—the study of the precise nature and quantitative distribution of the carbohydrate fractions in feeding stuffs.

The adoption of the herbivorous mode of life may be achieved in one of two ways. Either the animal makes use of what may be termed the normal complement of digestive enzymes—this would involve the consumption of a very large bulk of food; or else it must develop some means of digesting the bulky components of the diet—the insoluble cellulose, the hemicellulose and pentosans—thus cutting down the mass of food needed.

The herbivores have adopted the latter alternative and have made use of digestion, or rather fermentation, by means of micro-organisms. Of the herbivores, the ruminants are the most efficient and they can digest from 50% to 70% of the insoluble material in the diet, depending on nature of the diet.

The next question is what does the ruminant obtain as a result of bacterial digestion? It obtains three groups of substances: (a) Volatile fatty acids; (b) B group of vitamins; (c) micro-organisms. The total amount and fate of each of these three groups is important. At the moment we only have precise data on the first of these groups, the volatile fatty acids. Generally speaking, it is true to say that the volatile fatty acids in the rumen consist of acetic, propionic and butyric acids in the proportion of 70:20:10 respectively. Further, these fatty acids are absorbed into the blood-stream through the wall of the rumen and are metabolized by the animal, only a very small proportion being excreted in the urine. From studies of the rate of absorption, it is possible to state that at least 1/6th of the animal's calorific requirements are obtained in the form of volatile fatty acids. It has also been possible to show that the contracting heart can utilize acetic acid as fast as it consumes glucose; on the other hand, our knowledge of the detailed metabolism of these simple compounds is at the moment fragmentary, and would well repay study. It is also important to note that in the rumen no free reducing sugars can be observed, and 100 grammes of glucose can be added direct to the rumen of the normal animal without causing a rise in blood sugar; instead the glucose is fermented very rapidly in the rumen and is converted to volatile fatty acids and lactic acid; while the former are absorbed the latter is not but instead undergoes a further fermentation to volatile fatty acids.

Our knowledge of the production of the B group of vitamins in the rumen is not so complete as that of volatile fatty acids. All that can be said at the moment is that the micro-organisms synthesize the B group far in excess of their own requirements and that in this way the quantity of this group of substances available to the animal is increased. In individual cases, a tenfold increase has been observed in the amount of a given vitamin available to the animal, as a result of bacterial action in the rumen. There is great

scope for further study here and the application of the new methods of microbiological assay now being developed should yield valuable results.

The precise value to the animal of the micro-organisms, apart from their action as agents of digestion, is a matter of conjecture. We have no knowledge of the total weight of micro-organisms produced *per diem*. There is ample evidence in support of the view that part at least of the protein of the diet can be replaced by simple nitrogenous compounds such as ammonium sulphate or chloride, or urea, implying that the micro-flora can make use of these simple compounds in the synthesis of protein which is subsequently utilized by the animal; or, in other words, bacterial and protozoal protein is digested by the animal lower down the alimentary canal. But we have no quantitative data as to the nutritional value of the micro-organisms *per se*, because we do not know the rate of production. Until this data is obtained, it is idle to speculate in any save qualitative terms. This then is a problem of major importance. It is also pertinent to remark that we do not know what happens to the protein of the diet, whether it is converted into bacterial and protozoal protein, or whether it is hydrolysed to amino acids which are absorbed or fermented. The whole problem of protein digestion in the rumen is shrouded in mystery.

The next problem is the nature of the flora and the analysis of it. What are the functional organisms present? That is to say, what are the organisms which are playing an active part in the digestive processes occurring in the rumen, as opposed to those which may be called contaminants? I suspect that, given enough patience, it would be possible to isolate species of almost every family known. It is not sufficient, therefore, to isolate organisms from the rumen; an isolation by itself tells us nothing, unless it can be shown that the organism is playing an active part in digestion. If this rule is not obeyed, an isolation by itself becomes merely an exercise in micro-biological technique rather than a contribution to the study of ruminant digestion. This calls for the closest co-operation between the micro-biologist and the biochemist. So far, only two organisms have been isolated which obey these criteria, an iodophile coccus, and members of the genus *Propionic bacterium*.

A second feature of the microbial population of the rumen is the constancy of its products no matter what the diet, and, at the same time, the dependence of the population on the nature of the diet. It can be readily observed that certain changes in the population occur when the diet is changed. These observations have been made by direct microscopic examination. It may well be that the fundamental organisms do not change, and that such changes as are observed are of little importance. But, none the less, the changes are very marked; on one diet rich in sugars, e.g. mangolds, very large numbers of a pseudo-yeast can be seen; change to a starchy diet, and the yeasts disappear and in their place are iodophile cocci. These observations raise the following question: what are the factors concerned in maintaining a constant population and how does the population protect itself, from the animal's point of view, against invasion by harmful organisms? This brings us down to the necessity for a study of the principles of bacterial ecology. For too long now have bacteriologists been content to isolate organisms in pure culture, neglecting the very important fact that in nature one finds mixed populations rather than pure cultures. Such studies applied to the rumen, would yield results of value and put on to a rational basis the well-known observation that dramatic changes in the diet of ruminants upset the animal.

In conclusion, I wish to emphasize that such work as has been done on ruminant digestion is only a start; there is a great need for chemists, physiologists, biochemists and microbiologists to take up the study of the digestive processes of the ruminants, which after all form our most important group of domestic animals.

Dr. A. T. Phillipson: Fermentation, as a means of digestion, is not confined to ruminants; other animals such as the horse, pig, rabbit and rat are known to produce the same fatty acids in their large intestines as those produced by bacterial fermentation in the rumen. In addition the dog can now be added to the list for acetic and propionic acids are now known to be present in the digesta of the colon in concentrations which compare with the concentrations found in the large intestines of other animals. Alimentary fermentation, therefore, is quite a widespread process but its importance relative to digestion by enzymes of glandular origin varies in different species and, as far as one can tell at present, it is in the ruminant that it assumes the greatest dimensions.

One remarkable feature of digestion in the rumen is that bacteria that are detrimental to the host do not flourish in spite of the fact that conditions for anaerobic bacterial growth are ideal. One is forced to ask the question whether this state of affairs always exists or whether it is possible that under certain circumstances, such as a change of

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Mr. A. Brownlee: Observations on stall-fed cattle show that these animals follow a fairly regular routine in their rumination habits. After a meal there is usually a period lasting twenty minutes or longer during which the animals do not ruminate. Rumination then commences and continues for a period averaging about twenty-eight minutes. This period is followed by a non-ruminating period averaging about thirty-eight minutes, to be followed by alternate similar periods of rumination and non-rumination until the next feeding time approaches. In a heifer fed strictly twice per day, eleven such ruminating periods were observed to occur between an evening and a morning feed.

During the non-ruminating periods cows swallow saliva at the rate of about $1\frac{1}{2}$ swallows per minute. In a sheep which was destroyed and the abdomen opened without delay, the reticulum was found to be filled with fluid contents in contrast to the more solid contents of the rumen. It would have been interesting to know if this fluid was saliva. Attempts to confirm this observation in slaughterhouse material have so far been unsuccessful.

The following observation was made on cows grazing during daytime and housed at night. At the time of observation most of these animals had been grazing continuously for a period of at least three hours on good aftermath about half eaten down. A number of animals then drank water and almost immediately several of them commenced to ruminate. Most of these stifled the rumination reflex and recommenced grazing.

Dr. F. H. Malpress: Dr. Owen has remarked that the absorption of large quantities of the lower fatty acids from the rumen might be related to the presence of lower fatty acids in large amounts in the butter-fat of ruminants. He may be interested to know that work is already in progress at N.I.R.D., Shinfield, designed to investigate any such relationship. The aim of the initial experiments has been to show whether it is possible to modify the characteristic changes in the fatty acid content of butter-fat, known to attend the starvation of lactating ruminants, by coupling starvation with the intravenous infusion of salts of the lower fatty acids. The work is incomplete and as yet inconclusive, but already there are grounds for believing that such modification is possible and that the mammary gland can utilize circulating fatty acids of this type to some extent in the formation of milk-fat.

Mr. G. N. Gould: My contribution to the discussion will be from the clinical aspect and will deal with the problem of "bloat". Although it has been possible by the use of the ley system markedly to increase productive value of pasturage, problems have arisen of great importance and interest to veterinarians and agriculturists. One of the most important is the tendency to "bloat" which has been frequently responsible for deaths in cattle grazed on leys.

One system of management which is claimed to be valuable in prevention, is for the cattle to be turned on to the leys for a comparatively short period and then removed to a straw yard or bare pasture. This, not infrequently, proves satisfactory but involves not only considerable organization but also labour which is at a minimum on most farms to-day and which, moreover, is expensive.

I have recently had a most interesting experience with a herd of pedigree Jersey cows which tends to demonstrate the possibility of the psychological aspect being worthy of

diet, the stability of the flora is upset and that bacteria detrimental to the host make their appearance in quantity, or alternatively, that organisms which normally produce useful materials elaborate materials harmful to the host, due to change in environment. The condition known as "Bloat" is one instance in which something of this nature may be happening. Death in bloat is attributed to pressure of gas in the rumen impeding either or both the circulation and respiration. There is no experimental proof, however, to show that pressure as such in the rumen will seriously interfere with either of these systems and there is no evidence to show that the pressures that have been recorded in living bloated animals are lethal. Until this question is settled there is good reason to suppose that some other factor is concerned and that bacterial products other than gas are produced and absorbed from the rumen under the influence of the sudden change of diet which occurs when animals are turned on to leguminous pastures. Bloat is only one instance of the conditions which are open to investigation on these lines but it is necessary that more be known of the normal processes of digestion in the rumen before much progress can be made in this direction and for this reason, apart from the nutritional problems involved, the study of digestion, and particularly of the microbiology of the rumen, is important.

Dr. E. C. Owen: I have just completed a review of the literature of ruminant nutrition. I had been looking especially for evidence as to the exact role played by bacteria in digesting cellulose but I found that the chemical evidence on this point was far from satisfactory. Kellner's experiments with cellulose and numerous other more recent observations make it certain that the ruminant digests a considerable proportion of the cellulose it ingests.

Microscopic observation of rumen contents [1] gives circumstantial evidence that certain cocci are cytotactic while other observations in the living animal show that cellulose digestion in the ruminant was not confined to the rumen. It also occurs in post-abomasal regions of the gut [2]. I agree with Dr. Elsdén that biochemically satisfactory evidence as to the organism or organisms in the rumen which are responsible for the breakdown of cellulose is still lacking. Organisms have been isolated from rumen contents and have been found to be able to break down cellulose, but the conditions under which the breakdown occurs are not comparable to conditions obtaining in the rumen. There is a danger too, that a specific bacterium isolated from the rumen is merely a passenger therein. For this reason microscopically controlled cultures of mixed rumen flora are more likely to reflect the conditions in the rumen than are cultures of isolated bacteria, particularly if plating be used for the isolation. Such objections apply to the work of Pochon [3] whose organism *Plectridium cellulolyticum* was a spore-former isolated by plating. Pochon found it in rumen contents at pH 8, a pH too alkaline to be considered as normal.

Dr. Elsdén has drawn attention to the importance of acetic acid as a product of the fermentation which occurs in the rumen and of which he and his colleagues at Cambridge are making an intensive study [4]. There has recently been a revival of interest in America as to the role of acetic acid in intermediary metabolism. Work with heavy and with radio-isotopes has shown that acetic acid can form both fat and glycogen in the liver and body tissues and that it is an important precursor of cholesterol.

In the rumen acetic acid is formed from carbohydrates such as starch and sugar. It still remains to be shown to what extent cellulose in the rumen is responsible for acetic acid production.

The generation of acetic and other lower fatty acids in the rumen may have a bearing on the origin of the lower fatty acids of milk fat, an outstanding problem in the metabolism of milk secretion. Hilditch [5] has arranged 13 different species of mammals in the order of increasing concentration of lower fatty acids. An examination of this table of species from a biological standpoint is very interesting. It so happens that a carnivore, the dog, heads the list with the lowest value. After the dog come the omnivora, pig, man and mouse. Next come the herbivora, horse, ass and rabbit, while last of all with the greatest values come the ruminants, camel, goat, sheep, buffalo and cow.

It is tempting to suppose that the extent of generation of acetic acid and other simple fatty acids in fermentations due to bacteria inhabiting the gut is responsible for the increase of lower fatty acids in the milk as one passes from the dog to the cow.

Contrary, however, to such a hypothesis is the hypothesis of Hilditch that the lower fatty acids in the milk originate from the unsaturated fatty acids, such as linolenic, which

are abundant in grass so that if the lower fatty acids of the milk of an animal reflect its grass intake the order of species in Hilditch's table would be satisfactorily explained.

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Dr. F. H. Malpress: Dr. Owen has remarked that the absorption of large quantities of the lower fatty acids from the rumen might be related to the presence of lower fatty acids in large amounts in the butter-fat of ruminants. He may be interested to know that work is already in progress at N.I.R.D., Shinfield, designed to investigate any such relationship. The aim of the initial experiments has been to show whether it is possible to modify the characteristic changes in the fatty acid content of butter-fat, known to attend the starvation of lactating ruminants, by coupling starvation with the intravenous infusion of salts of the lower fatty acids. The work is incomplete and as yet inconclusive, but already there are grounds for believing that such modification is possible and that the mammary gland can utilize circulating fatty acids of this type to some extent in the formation of milk-fat.

Mr. G. N. Gould: My contribution to the discussion will be from the clinical aspect and will deal with the problem of "bloat". Although it has been possible by the use of the ley system markedly to increase productive value of pasturage, problems have arisen of great importance and interest to veterinarians and agriculturists. One of the most important is the tendency to "bloat" which has been frequently responsible for deaths in cattle grazed on leys.

One system of management which is claimed to be valuable in prevention, is for the cattle to be turned on to the leys for a comparatively short period and then removed to a straw yard or bare pasture. This, not infrequently, proves satisfactory but involves not only considerable organization but also labour which is at a minimum on most farms to-day and which, moreover, is expensive.

I have recently had a most interesting experience with a herd of pedigree Jersey cows which tends to demonstrate the possibility of the psychological aspect being worthy of

consideration. This herd of thirty-six high pedigree cows and heifers, had, from the beginning of April, been grazing on a ley consisting of rye grass, cocksfoot and S.100 clover. When first turned out there was a luxuriant growth with the grasses standing well above the clover. For the first week the herd was grazed for one hour twice daily, and there was no trouble, but it was noticeable that they "skimmed" the surface of the pasture taking mainly the grasses standing above the clover. When they reached the clover the trouble started, and from time to time cows became blown. One was lost—dying within half an hour of the condition being noticed, three-quarters of an hour after the animal had left the pasture and been placed in a practically bare milking yard.

The period of time was then reduced to three-quarters of an hour, but blowing continued to occur with monotonous regularity. In turn other cows in the herd were affected, and it was not uncommon to find anything between nine to fifteen cows in various states of "bloat". The period was gradually reduced until it became twenty minutes' grazing twice daily.

A change on to another re-seeded pasture consisting of S.100 clover, some wild white clover, cocksfoot, rye grass and old pasture grasses, caused exactly the same results, and as the farm was one in which there was no permanent pasture left and little or no hay available, the condition had really become desperate. Hay and straw were provided for the cattle before they went to pasture and at pasture, but they were steadfastly refusing to eat it, and the tendency to "bloat" continued. This had previously proved to be a satisfactory preventive measure on other farms, provided the cows would eat the straw and hay.

In the owner's absence abroad, the management of the herd passed over to me, and on the first night fifteen cows were blown within half an hour of being moved from the ley after twenty minutes' grazing. I decided to move the whole of the cows from the ley and put them in the collecting yard and change them over on to full winter rations of hay and concentrates.

After a period of five days, six cows which had been frequently blown from the period April to June 1, were placed on the re-seeded pasture after giving them access to as much dry food as they would eat, in the way of hay and their usual production ration, following the afternoon milking. They were carefully watched and it was noticeable how greedily they ate with their heads down to pasturage the whole time. At the end of twenty minutes all the cows moved to the gate as if ready to leave the field, but they were left and a watch kept on them during the evening. All six appeared full but showed no evidence of "bloat". After thirty to forty minutes they lay down and ruminated and were left for the night. When they came in for morning milking they received a production ration and a small amount of hay, and were put out again and left until the afternoon milking. They ate less greedily and moved about more, but they came down to the gate at the end of twenty minutes. They were allowed to remain under supervision until the afternoon milking, and no trouble occurred, and the same procedure was followed subsequently.

After three days they gave up the habit of coming down to the gate at the end of twenty minutes, and dispersed themselves over the pasture much more than in the previous three days.

At that time six more cows were introduced and a comparison made in grazing methods. The six new cows showed the same tendency to greedy feeding with their heads down to the ground, and at the end of twenty minutes were waiting at the gate. The same procedure was again successfully followed, and ultimately all the cows in the herd were on the pasture and staying there for twenty-four hours on end, other than for the times they were taken in for milking, and the tendency to "bloat" had disappeared. It took three to four days in all cases for the cows to get over the habit of coming down to the gate as if waiting to be removed from the pasture. It was very noticeable that the cows, when first introduced, ate greedily with their heads down to the pasture all the time, and that they moved very little. Normally a cow will graze and lift its head frequently and move on. At the time of lifting the head, particularly on a luscious pasture, belching is frequently noticed. It would appear that in this particular case a psychological condition had arisen as a result of which the cows assumed the habit of eating as fast as they could in the shortest possible time, due to continued reduction in grazing period, and this was contributing to the tendency to "bloat" to a marked extent.

The change in management enabled the cows to graze full time on pastures which seven to fourteen days previously had been too dangerous to continue to use.

Section of Otology

President—A. J. WRIGHT, F.R.C.S.

[May 3, 1946]

At this meeting a paper by Messrs. Cope, Dix, Hallpike, Harrison, Hood and Lumsden, entitled "Some Experiences with the Establishment and Working of a Deafness Clinic" was read by Mr. Hallpike.

The subject matter of this paper will be found presented in full in the Report of the Electro-Acoustics Committee of the Medical Research Council.

(Publication of this Report by H.M. Stationery Office is expected shortly.)

Section of Otology with Section of Laryngology

COMBINED SUMMER MEETING HELD AT TORQUAY.

[June 14, 1946]

OTOLOGICAL SESSION

Chairman—A. J. WRIGHT, F.R.C.S.

(President of the Section of Otology)

Evidence for a Vascular Mechanism in Ménière's Syndrome

By MILES ATKINSON, M.D., F.R.C.S.

If histamine is injected into the skin, what Lewis called "the triple response" takes place: (1) a raised red area in the skin; (2) the rapid formation of a bleb, and (3) a surrounding area of erythema. This qualitative experiment can be turned into a quantitative test by injecting intradermally a known amount of histamine solution of known strength, and that is the basis of the histamine skin test. The injection, given into the skin of the volar surface of the forearm just below the elbow, consists of 0.05 c.c. of a 1/10,000 solution of histamine calculated in terms of histamine base, not in terms of one of the salts. If this quantity is injected into the forearm there appears within a minute or so in the normal subject a raised red area and, following this, the rapid formation of a yellow bleb surrounded by an area of erythema. That yellow bleb in the normal subject is from 1/4 in. to 1/3 in. across, and the area of erythema surrounding it from 1 in. to 1½ in. in diameter. The reaction remains like that for from five to ten minutes and then begins to fade. In twenty minutes the bleb has faded into the

consideration. This herd of thirty-six high pedigree cows and heifers, had, from the beginning of April, been grazing on a ley consisting of rye grass, cocksfoot and S.100 clover. When first turned out there was a luxuriant growth with the grasses standing well above the clover. For the first week the herd was grazed for one hour twice daily, and there was no trouble, but it was noticeable that they "skimmed" the surface of the pasture taking mainly the grasses standing above the clover. When they reached the clover the trouble started, and from time to time cows became blown. One was lost—dying within half an hour of the condition being noticed, three-quarters of an hour after the animal had left the pasture and been placed in a practically bare milking yard.

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Intramuscular injections may have to be continued for many months, as there is, for a long time, danger of relapse unless treatment is continuous.

After showing audiograms of cases, Dr. Miles Atkinson summed up by saying: The histamine skin test divides Ménière patients into two groups: histamine-positive and histamine-negative, the first being a small group and the second large, in the proportion of about 1 to 5 or 6. The histamine-positive group is best treated with histamine desensitization and responds extremely well, so much so that I used to say that to get a positive reaction to histamine was as much a prognosis as a diagnosis. The other, the bigger group, should be treated with vasodilators, of which nicotinic acid has proved in my hands the best. They respond well, and if one is patient and persistent there are very few cases which cannot be got under control by medical treatment.

Mr. V. E. Negus said that he had been interested in histamine and its effects, particularly as regards the nasal aspect of the allergic reaction. The latter was merely a peculiar response of the tissues and could be caused by the breaking down of histidine. If histamine were released, œdema was produced, due to capillary dilatation and the increased permeability of cell walls, with increase of fluid in the tissue spaces. The œdema could be reduced by calcium, or by the driving in of hydrogen ions by ionization. Very often an allergen was not found in typical nasal allergy, nor was it found in cases of chronic nasal œdema. It did not mean that because a skin reaction was not found there was not something at work similar to the allergic reaction, which could produce these changes.

A large number of patients were treated for sinusitis because they had pains in the head and temporal region, and one of the popular methods of treatment was by displacement. Even in the case of such rheumatic affections, œdema of the muscles of the lumbar region, as a result of physical allergy, had been found causing pressure within the muscle sheaths and causing the pain of lumbago.

Dr. John Freeman, who had done a great deal of work on allergic conditions, laid great stress on the factor of response to bacterial growth. In the treatment of many conditions due to organisms the occurrence of secondary allergic effects could be brought about. Many skeletal muscles and joints gave an allergic response, and for his own part he did not see any great difficulty in agreeing with the theory of indirect bacterial causation. Professor Atkinson's interesting talk on hypo-sensitization with histamine seemed to fit in very well with other theories of allergic reactions.

He had recently been interested in seeing an elderly lady who first came to him in 1938 complaining of sudden and almost complete deafness in her right ear. She had no vertigo or signs of hæmorrhage and her labyrinth was well functioning. Various investigations were carried out. About three weeks ago she came again with exactly the same condition in the other ear—sudden deafness with very severe tinnitus, but no vertigo. The cochlea was found to be depressed over all ranges. There was obviously a cochlear deafness. The caloric reactions showed that the labyrinths were both functioning. He got some insight into the condition on reading a paper showing that the changes of Ménière's disease might start in the cochlea. The cochlea might be regarded as a "shock" organ, just as allergists spoke of other organs of the body as shock organs. He gave this lady ammonium chloride to fix salt, and she now wrote to say that she was much better—the tinnitus had diminished until it was tolerable, and so far as the deafness was concerned she was now able to hear the wireless.

He had been interested in seeing a Report on the use of benadryl from the Mayo Clinic. He wondered whether this was likely to be of use in cases of primary aural vertigo.

Ménière's Disease—A Critical Review

By A. J. WRIGHT, F.R.C.S.

SOME nine years ago I first contributed a paper on this subject to this Section (*Proc. R. Soc. Med.*, 1937, 31, 87). Since that time two outstanding advances in our knowledge of Ménière's disease have been achieved in that both the clinical and pathological pictures have been defined and we now regard Ménière's disease as an entity. The fundamental cause of the disease is as yet unproven.

Clinical picture.—(1) Ménière's disease occurs in individuals at all ages and is not obviously associated with any other gross constitutional disturbance.

(2) Two types which perhaps are distinct can be recognized. The more usual one in which the lesion is essentially unilateral, and the less common one in which it is bilateral and approximately equal from the beginning. The latter cases tend to be more rapid in development and more resistant to treatment and remain for further investigation.

(3) The first signs of the disease are usually associated with the cochlea and it may possibly be of significance that this contains the vascular area which is probably in the main responsible for the secretion of endolymph.

(4) As a corollary to this many cases of perceptive deafness are explainable as being the initial stages of the disease and these are I believe usually recognizable.

surrounding erythema and in half an hour or so the whole thing has disappeared save for a little mark at the point of injection which may remain for twenty-four hours. That relates to the histamine-negative or—insensitive subject.

The histamine-positive or sensitive subject gives the same reaction as the normal except that it is much larger. The bleb measures from $\frac{3}{4}$ in. to 1 in. across, sometimes even more, while the surrounding erythema may be as much as 2 in. to $2\frac{1}{2}$ in. across. But the outstanding characteristic is the appearance of a long trailing pseudopodium from 1 in. to $1\frac{1}{2}$ in. in length. This represents a lymphatic made evident by the histamine. There may even be two pseudopodia if two lymphatics are available at the site of injection to be marked out by the histamine.

Between these two extremes of the negative or insensitive and the positive or sensitive there are intermediate stages which require a certain amount of judgment and experience to evaluate.

The treatment of the two groups is quite different, and it is therefore important to form an accurate assessment of the group to which each patient belongs, whether negative or positive. If in doubt, one should undertake a second test with double the dose, using preferably the opposite forearm and leaving an interval of forty-eight hours for the reactionary period. If with that double dose no pseudopodium appears one can be satisfied that the case is histamine-insensitive.

What does this mean? Histamine is a vasodilator substance. If injected intravenously in sufficient dosage a marked flushing of the face occurs. Therefore, when these two classes of cases were discovered, it was assumed that the one that gives the large response, the histamine-positive, does so because it possesses a primary vasodilator mechanism. The other, the histamine-negative group, was assumed to possess a primary vasoconstrictor mechanism. If these assumptions are correct, those patients who give a positive response to histamine should be made worse by vasodilator drugs and better by vasoconstrictor drugs; while in the histamine-negative group precisely the reverse should occur. This is, in fact, what happens.

If a member of the histamine-positive group be given amyl nitrite to inhale, the result may be an attack and, nearly always, at least a vestibular response. The same thing will happen with other vasodilator drugs. Recently a histamine-positive patient was inadvertently given an intravenous injection of 35 mg. of nicotinic acid. A very considerable flush response resulted. About one hour later she had as severe an attack of Ménière's syndrome as she had ever had in her life. That is not an isolated instance; the same result has been observed many times following the mistaken administration of a vasodilator drug to a histamine-positive patient.

In the insensitive group, if the patient is given one of the vasoconstrictors such as ergotamine tartrate or benzedrine it is frequently possible to produce an attack or even a succession of attacks, while the patient can be swung out of an attack sometimes by giving amyl nitrite.

The speaker here showed by means of a diagram the results of treatment in the two groups. Briefly, the histamine-sensitive group had been found to be best treated by histamine-desensitization—gradually increasing doses of histamine given subcutaneously. The results have been very satisfactory. The method is to start with the same dose subcutaneously as was given for testing intracutaneously and gradually work up. Two audiograms were shown demonstrating improvement in hearing with correct treatment, deterioration with incorrect.

The same thing applied to the other histamine-insensitive group, but the other way round—correct treatment, using nicotinic acid as the vasodilator improved the situation, incorrect treatment produced deterioration.

The results in both groups as far as the attacks of vertigo were concerned were very satisfactory, about 80% being relieved or greatly improved. As far as tinnitus was concerned, about 50% are greatly improved; improvement in deafness is unusual, 20% or less.

The treatment of the larger group calls for patience and perseverance on the part both of the patient and the doctor. Our routine is to give nicotinic acid at first intravenously, starting with 25 mg. and increasing by 5 mg. a day until the maximum tolerance is reached somewhere between 50 to 100 mg. daily. After tolerance limit is established the same daily dose is continued intramuscularly and this the patient can be taught to give himself. At the same time, nicotinic acid is given orally in daily dosage of 150 to 300 mg.

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(2) Two types which perhaps are distinct can be recognized. The more usual one in which the lesion is essentially unilateral, and the less common one in which it is bilateral and approximately equal from the beginning. The latter cases tend to be more rapid in development and more resistant to treatment and remain for further investigation.

(3) The first signs of the disease are usually associated with the cochlea and it may possibly be of significance that this contains the vascular area which is probably in the main responsible for the secretion of endolymph.

(4) As a corollary to this many cases of perceptive deafness are explainable as being the initial stages of the disease and these are I believe usually recognizable.

(5) The most striking characteristic of the disease is its tendency to progress and to remit, such periods of remission not infrequently being of very long duration. This characteristic must be taken into account in any explanation as to the fundamental cause of the complaint.

(6) The occurrence of the vertigo in attacks is difficult of explanation. Possible explanations would seem to be: (a) A sudden obstruction to some portion of the membranous labyrinth giving rise to increase in tension, as we see in glaucoma. (b) The summation of stimuli leading eventually to an explosive response as we see in epilepsy and migraine. A combination of the above two factors is possible.

Pathological picture.—It is now established that the cause of the symptoms is to be found in a lesion in the labyrinth. The researches of Hallpike amply confirmed by others have shown, as a constant picture, a distension of the membranous labyrinth and perhaps some alteration in the constituents of the endolymph. Examination of the eighth nerve has not revealed any abnormality. That the symptoms are due to a lesion in the end-organ is also shown by the fact that its destruction or the severance of its nervous connexion with the brain will arrest the vertiginous attacks.

Theories as to the nature of the complaint.—The following considerable list has been put forward by different observers: (i) Eustachian obstruction with resulting secondary pressure changes in the labyrinth. (ii) Vascular dysfunction in the direction of spasm, dilatation, or alteration in the permeability of the capillary wall. (iii) Retention of water or electrolytes. (iv) Allergy. (v) A bacterial toxæmia.

A critical review of the above theories

Eustachian obstruction with resulting secondary pressure changes in the labyrinth: In my experience this is only found as a factor in causation when the labyrinth is itself pathological. This does not exclude the possibility of a vestibular disturbance as a result of abnormal pressure changes in the middle ear but such cases of eustachian block should not properly be included under the term Ménière's disease unless they present other evidence of a lesion in the labyrinth.

Vascular dysfunction: This may quite possibly take part in the mechanism of the complaint but does not offer any explanation as to the fundamental causation.

Retention of water or electrolytes: A similar statement can be applied to this theory. That there is a local retention of fluid in the membranous labyrinth is now proven, but I have never been able to satisfy myself that this is part of a constitutional dysfunction. That treatment directed to this factor should alleviate the symptoms is not surprising.

Allergy: By this I presume is meant a tissue reaction abnormal in degree or kind or both, to some circulating foreign substance whether bacterial or otherwise. We would expect that such increased sensitiveness might not uncommonly be present but I have been surprised to find how relatively infrequently general allergy is present in the victims of this complaint.

A bacterial toxæmia: This theory, whether correct or not, is the only one which suggests a fundamental cause for the complaint and is the one which I accept. My reasons for doing so are in the main that by its nature it would fit as a cause for a progressive but frequently remittent lesion and that, in my experience, elimination of such a factor tends to produce a remission. Most important of all, the probability of the production of such a remission seems to vary in direct relationship to the degree to which one can expect completely to eliminate the source of infection surgically; thus, for example, the most brilliant results are obtained by the extraction of a single dead or infected tooth in a young person in whom other sources of infection can be reasonably excluded.

Atkinson has recently described me as a lone figure in my support of the infective hypothesis.

I believe that I am the only worker in this field who has tried over a long period, and I hope, with some degree of scientific accuracy, to assess the truth of the infective causation.

Up to the present, as far as I am aware, only somewhat vague general statements have been made by others combating the infective hypothesis. I shall therefore continue in my belief until presented with the results of a similar investigation producing contrary findings.

Mr. E. D. D. Davis said that there was considerable evidence in favour of that theory such as the sudden explosive onset, fainting attacks and other vascular disturbances, and the increased intra-labyrinthine pressure which might explain the dilatation of the

canal of the cochlea, discovered by Hallpike. It was significant that vasodilators could produce an attack of Ménière's syndrome.

The President had mentioned eustachian obstruction. He himself had not found that eustachian obstruction had produced a true Ménière's syndrome. All the cases of true Ménière's syndrome which he had seen had a remarkably patent eustachian tube as shown by the eustachian catheter.

He thought that sepsis may be a contributory cause and there were cases which improved after the drainage of a suppurating antrum or nasal sinus. On the other hand, the extraction of teeth, enucleation of tonsils and the removal of other septic foci had no appreciable beneficial effect on the vertigo in all cases.

Mr. C. P. Wilson, who said that he had been interested in this subject for a long time, desired to ask Professor Miles Atkinson whether there was not, in addition to the positive and negative groups, a third histamine group, in which the findings were equivocal. The sensitive people were of the type who some years ago were classified as of the vagotonic type. They might properly be called potential allergics. There was a large group of normals who were not in one group or the other: their reactions were equivocal. The other interesting point about these cases was that the majority of the histamine-sensitive people had a very low blood-pressure, and they had a distinct family history of longevity. If one inquired into the family history it was rare not to find a relative who had lived to something like 85.

Mr. C. Hamblen-Thomas asked whether he was to understand that eustachian obstruction was not a factor in vertigo. He had always considered it to be a large factor.

Mr. H. V. Forster said he had rarely been able to discover a focus of sepsis responsible for vestibular vertigo in Ménière's syndrome, though he would look upon a devitalized tooth with suspicion.

In the earlier years of this century it had been the custom to indict the large bowel as a source of toxic absorption and a menace to man's longevity.

When, however, one thought of the elaborate chemical processes attending digestion in the small intestine, it might be left to the imagination to consider the consequences when these were disturbed.

He did not think that in civilian practice impaired ventilation of the eustachian tube often accounted for our cases of vestibular vertigo.

Mr. Stirk Adams considered a central disturbance in the mid-brain nuclei could produce all the symptoms of a unilateral labyrinthine vertigo, and quoted two cases in support of this thesis.

The first occurred to a doctor, twenty-five years ago, who developed a devastating attack of vertigo which persisted for six weeks. For the whole period of the attack a spontaneous nystagmus prevented fixation of external objects, but after the attack subsided, all symptoms disappeared and no deafness has ever appeared in either ear. There has been no recurrence.

He had heard of a second case, in which recurrent unilateral labyrinthine attacks had ultimately been treated by surgical destruction of the labyrinth, but this failed to give relief. The attacks disappeared, however, when the patient gave up smoking.

Dr. Miles Atkinson, in reply, confessed that he was not so sceptical of the idea of sepsis being a factor as he had formerly been; nevertheless, he was not ready to accept that as the whole explanation. He regarded Ménière's syndrome as consisting of the triad of symptoms, vertigo, tinnitus, and deafness, all three together. He was not prepared as yet to accept anything short of that. Mr. Davis had said that he always found an open eustachian tube, and he (the speaker) agreed, though undoubtedly a sudden block could produce acute vertigo temporarily. As for the incidence of associated migraine, he had seen a number of such cases. In fact, in his view one of the commonest associated symptoms of Ménière's syndrome was headache, and this was sometimes of true migraine type. Sometimes the Ménière attacks replaced the migraine attacks, so that with the first attack of vertigo the headaches ceased. He had had patients who had suffered with migraine for many years who had said: "When my dizziness started my headaches ceased." Here was another piece of evidence which tended to support the vascular thesis.

Mr. Wright had said that the vascular thesis, however good or bad, did not explain what was at the back of it all, and Mr. Wilson had forestalled him by suggesting three groups instead of two. He agreed with both speakers. He could do no more here than suggest that the basic fault is a metabolic one, admittedly a very broad term. For instance he had been doing some investigation into metabolic processes in this condition and he could say that a high blood cholesterol content had been found in many cases, whatever that may signify. In his view—he was coming to it gradually, and he thought there was a good deal of evidence for it—there was a profound metabolic disturbance which prevented the adequate utilization of vitamins and/or other nutritional factors. This metabolic disturbance could be induced by several different factors, one of which undoubtedly might well be the chronic infective focus upon which Mr. Wright was so insistent.

Mr. A. J. Wright said that he fully appreciated that there was no quarrel as between Mr. Atkinson's position and his own. Each of them might have got hold of different aspects of the same truth. He had already drawn attention to the fact that in these cases one did occasionally get a sudden onset of deafness which was difficult to explain. The occurrence of this condition in one ear and at a later date in the other was not, unfortunately, rare. There were points worth considering in this connexion, such as the extremely minute size of the membranous labyrinth. Again, there was evidence in Hallpike's work of an alteration in the endolymph, so that what was a clear fluid-like aqueous

(5) The most striking characteristic of the disease is its tendency to progress and to remit, such periods of remission not infrequently being of very long duration. This characteristic must be taken into account in any explanation as to the fundamental cause of the complaint.

(6) The occurrence of the vertigo in attacks is difficult of explanation. Possible explanations would seem to be: (a) A sudden obstruction to some portion of the membranous labyrinth giving rise to increase in tension, as we see in glaucoma. (b) The summation of stimuli leading eventually to an explosive response as we see in epilepsy and migraine. A combination of the above two factors is possible.

Pathological picture.—It is now established that the cause of the symptoms is to be found in a lesion in the labyrinth. The researches of Hallpike amply confirmed by others have shown, as a constant picture, a distension of the membranous labyrinth and perhaps some alteration in the constituents of the endolymph. Examination of the eighth nerve has not revealed any abnormality. That the symptoms are due to a lesion in the end-organ is also shown by the fact that its destruction or the severance of its nervous connexion with the brain will arrest the vertiginous attacks.

Theories as to the nature of the complaint.—The following considerable list has been put forward by different observers: (i) Eustachian obstruction with resulting secondary pressure changes in the labyrinth. (ii) Vascular dysfunction in the direction of spasm, dilatation, or alteration in the permeability of the capillary wall. (iii) Retention of water or electrolytes. (iv) Allergy. (v) A bacterial toxæmia.

A critical review of the above theories

Eustachian obstruction with resulting secondary pressure changes in the labyrinth: In my experience this is only found as a factor in causation when the labyrinth is itself pathological. This does not exclude the possibility of a vestibular disturbance as a result of abnormal pressure changes in the middle ear but such cases of eustachian block should not properly be included under the term Ménière's disease unless they present other evidence of a lesion in the labyrinth.

Vascular dysfunction: This may quite possibly take part in the mechanism of the complaint but does not offer any explanation as to the fundamental causation.

Retention of water or electrolytes: A similar statement can be applied to this theory. That there is a local retention of fluid in the membranous labyrinth is now proven, but I have never been able to satisfy myself that this is part of a constitutional dysfunction. That treatment directed to this factor should alleviate the symptoms is not surprising.

Allergy: By this I presume is meant a tissue reaction abnormal in degree or kind or both, to some circulating foreign substance whether bacterial or otherwise. We would expect that such increased sensitiveness might not uncommonly be present but I have been surprised to find how relatively infrequently general allergy is present in the victims of this complaint.

A bacterial toxæmia: This theory, whether correct or not, is the only one which suggests a fundamental cause for the complaint and is the one which I accept. My reasons for doing so are in the main that by its nature it would fit as a cause for a progressive but frequently remittent lesion and that, in my experience, elimination of such a factor tends to produce a remission. Most important of all, the probability of the production of such a remission seems to vary in direct relationship to the degree to which one can expect completely to eliminate the source of infection surgically; thus, for example, the most brilliant results are obtained by the extraction of a single dead or infected tooth in a young person in whom other sources of infection can be reasonably excluded.

Atkinson has recently described me as a lone figure in my support of the infective hypothesis.

I believe that I am the only worker in this field who has tried over a long period, and I hope, with some degree of scientific accuracy, to assess the truth of the infective causation.

Up to the present, as far as I am aware, only somewhat vague general statements have been made by others combating the infective hypothesis. I shall therefore continue in my belief until presented with the results of a similar investigation producing contrary findings.

Mr. E. D. D. Davis said that there was considerable evidence in favour of that theory such as the sudden explosive onset, fainting attacks and other vascular disturbances, and the increased intra-labyrinthine pressure which might explain the dilatation of the

The cases in Group A are all cases which have been treated during the last few months. Previously it was not felt justifiable to use penicillin in such cases, and in any event, in previous cases, incision of the tympanic membrane was done as a routine if perforation had not already occurred: these were cases in which there was temperature, pain and redness of the drum but no marked bulging, and were the type of case in which one might have incised the drum had one seen the patient at his own home or some distance away while, if in hospital, one would perhaps have said "do a paracentesis tomorrow if the condition deteriorates"—in other words, they were the cases which one would not consider to be a simple acute catarrh but cases of early suppurative otitis media. Cases which showed definite bulging were always incised and come into Group B. Group C were cases which presented definite clinical or radiological signs of mastoiditis.

All cases were treated with intramuscular injections, 23 cases during the earlier period were given 20,000 units four-hourly while 87 have been treated by doses of 60,000 three-hourly. The smallest total dose given was 600,000 units while in one or two cases nearly 7 million units have been given. 7 cases treated with the smaller doses required a second course and also one case treated with the larger dosage.

It has not been easy to dissect the statistics to be obtained from these cases as one could divide them up into multitudinous groups, in fact into nearly 110 groups, as practically no two cases were exactly alike but I have endeavoured to obtain the maximum amount of useful information that was possible.

The numbers are so small that they must in many respects be misleading and I give the actual figures without suggesting that too much reliance is placed on any percentage shown.

All the cases could be considered as acute cases although in 15 there was a possibility of the condition being labelled as acute on chronic as there was a previous history of suppuration and swabs taken from the discharge showed secondary organisms—while in 5 other cases secondary organisms were present although there had been no history of previous trouble with the ears.

Six of the cases treated were those of acute infection following traumatic perforation of the drum and these accounted for 4 of the cases which grew secondary organisms. In 25 of the cases sulphonamides were also given as part of the treatment while in 85 cases no sulphonamides were used. Of these 25, 10 were in Group B out of 50; 15 were in Group C out of 42.

The second table shows the type of infection present.

TABLE II.

Group	No.	Nil	Strep.	Staph.	Pneumo.	Others	Secondary organisms present
Group A	18	18					
Group B	50	2	26	10	6	6	16
Group C	42	1	20	9	12	—	4
		21	46	19	18	6	20

The case in Group C in which no organisms were found was an acute influenzal ear which showed intense congestion of drum and marked mastoid tenderness with dullness of the mastoid on X-ray. This was treated by penicillin only without myringotomy and cleared up completely without perforation of the tympanic membrane. It is included in Group C and not in Group A.

Cultures were taken daily while discharge was present and subsequently every other day until the tympanic membrane had healed. Discharge was seldom present after the fourth day and in most cases it was not possible to grow organisms after the second day, and in many cases indeed not after the first day.

These figures conform roughly to those generally found and would vary within wide limits in any series of cases of this size, particularly if they included cases associated with any epidemic infection.

Dosage.—Much of the work, especially in the early stages, was experimental but the cases taken as a whole seem to show quite definite tendencies. The average doses given for the various groups and organisms are as shown in Table III.

TABLE III.

	Nil	Strep.	Staph.	Pneumo.	Secondary organisms
Group A	2,500				
Group B		2,000—	2,000+	2,800	3,100
Group C		2,000—	2,500+	2,650	5,850
		"000" omitted.			

material assumed different consistency. Given those two things, it was a perfectly simple mechanical proposition that there should be from time to time a sudden obstruction of the cochlea; in fact the connexion between the cochlear and the vestibular apparatus was on the most minute scale and that, in some cases, the one should become cut off from the other was, to his mind, rather to be expected than the reverse.

Mr. Davis and he saw the world through different spectacles. Mr. Davis, he thought, had made the sweeping statement that in the vast majority of cases of Ménière's disease no focus of infection could be found. He could not agree with broad statements of that sort. Mr. Wilson had mentioned low blood-pressure. Years ago vertigo was put down to high blood-pressure until people actually began to take the pressures and came to a different view. Mr. Forster had pointed out that the intestinal tract could lead to many ills in this connexion; also that under extremely abnormal conditions of pressure a vestibular disturbance could be produced, particularly if the middle-ear adjusting mechanism was not as it should be.

Mr. Stirk Adams had suggested that some cases were not labyrinthine. He thought that what he meant was that some cases of vertigo were not Ménière's disease. He wondered what evidence there was that the actual attack was not initiated in the labyrinth. In the picture of this disease one first got an alteration of one labyrinth. It was "sensitized" for a variety of reasons. The "sensitized" labyrinth might be damaged by something which would not have caused upset to a normal one. Occasionally it was an injury. He had known on two or three occasions the thermal factor to come in, such as with undue exposure of one side of the head—a long drive in winter with the window of the car open on that side. Given that change, one presumed a circulating factor which produced this reaction. Most frequently the circulating factor was a bacterial toxin, though that was not so in all cases.

Report on 110 Cases of Acute Infection of the Ear Treated With Penicillin

By C. P. WILSON, C.V.O., F.R.C.S.

I was in the fortunate position of being attached to one of those centres to which supplies of penicillin were allocated by the Medical Research Council at a very early stage in its use.

At first the supplies were very scanty and precious and we were able to use it only in certain specific types of case—particularly those cases which were resistant to sulphonamide therapy—and from an aural point of view we were limited to serious complications of mastoid disease such as meningitis. It was not until the supplies of penicillin became somewhat easier that we were justified in using it for purposes of research, in treatment of less serious cases such as uncomplicated mastoiditis and, later still, in simple acute suppurative otitis media. This limitation of use has restricted the number of cases which have so far been available to me and has also tended to vitiate any statistics which would include all cases, as during the first year these statistics would include only those cases associated with serious complications.

I have therefore not included 12 cases of acute infection of the ear with such complications as meningitis and apical petrositis although I have details of these cases with me and can refer to them if the subsequent discussion demands it.

In this present paper I am referring to a total of 110 cases treated with penicillin and before going any further would like to thank those of my colleagues who have allowed me to use the cases which have been under their care, particularly my colleague at the Middlesex Hospital, Mr. Monkhouse.

For convenience I have divided these cases into three groups:

- A. Consists of 18 cases of acute uncomplicated otitis media without perforation.
- B. Comprises 50 cases of acute suppurative otitis media in which spontaneous perforation occurred or in which the drum was incised, that is, discharging ears without definite signs of mastoiditis.
- C. Comprises 42 cases associated with a definite mastoiditis.

TABLE I.

	No. of cases	Secondary organisms present	Sulphonamides	Traumatic perforations
Group A	18	—	—	—
Group B	50	16	10	4
Group C	42	4	15	2
	110	20	25	6

Of those with secondary organisms { History of previous suppuration 15.
No history of previous suppuration 5.
Myringotomy was performed in 17 cases: 14 in Group B and 3 in Group C.
A mastoid operation was performed in 12 cases in Group C.

be greater than is necessary but in no cases of this group was a second course of treatment necessary. The one case of impaired hearing is in a child who had some degree of nasal obstruction and subsequent treatment of this condition has not, so far, improved the hearing.

Pain and temperature subsided very quickly, often within twelve hours but it is doubtful if this advantage compensates completely for having to have treatment for six days.

The dosage rather surprisingly has been greater than the average required for either streptococcal or staphylococcal infections in both Groups B and C and one cannot help feeling that the drainage provided by the perforation of the tympanic membrane is the main factor in reducing the dosage required. I think it would be reasonable to treat a group of similar cases with early myringotomy and compare the doses required.

I cannot help feeling that the main factor in the treatment of early acute infections of the ear still remains adequate drainage and if this does not occur naturally via the eustachian tube at a very early stage, incision of the drum is not favourably replaced by chemotherapy, either sulphonamide or penicillin.

In the other groups it is interesting to note that the pneumococcal infections needed considerably larger doses of penicillin than the others and those cases with secondary infections took, in some cases, huge doses and even so the results compare very unfavourably with simple strep. and staph. infections.

The great danger, to my mind, now that penicillin has become universally available is that it will be used by the general practitioner with the main object of providing the advantage of relief of acute symptoms and that once this object has been achieved there will be passive and even active resistance on the part of the patient or relatives to the continuation of treatment. This will, I fear, result in relapse with recurrence of the infection needing a subsequent course of treatment and worse still will turn the acute infection into a chronic or exudative otitis media with continued and permanent impairment of hearing.

It is this subsequent impairment of hearing which to my mind is the most serious danger which we will have to face and I cannot too strongly urge that even if all other symptoms have cleared up a case cannot be considered completed until the hearing has been restored to the best possible level.

We have had to face this problem during the last nine or ten years with the sulphonamides, and although it may be that penicillin presents considerable advantage in its efficiency, the very fact of its application being more unpleasant than the taking of tablets by mouth may produce for us the same problem but on a larger scale.

To sum up, penicillin is not *the* treatment of acute otitis media, it is an ancillary method. Treatment remains efficient drainage, and to the extent that by the use of penicillin these functions are reversed so great will be its menace.

The President said that he was pleased to note, on the one hand, the emphasis Mr. Wilson laid upon the question of hearing—which he was afraid they did tend rather to neglect—and, on the other, his warning against regarding a treatment because it was new as necessarily a substitute for anything one did in the past.

Mr. R. R. Simpson said that they had listened to some very impressive figures that morning, and he wanted to congratulate Mr. Wilson on his accurate and critical analysis of these cases. In the Services he himself had not been so impressed with the efficacy of penicillin in acute otitis media but he realized the important difference in his figures from those brought forward by Mr. Wilson. In dosage he had used 20,000 units instead of Mr. Wilson's 60,000, and since listening to him he wondered whether in the secondary infection type of case where massive doses had to be given they could not consider proceeding along the same lines of massive dosage as in gonorrhoea, e.g. 300,000. Mr. Wilson's figures certainly made him feel like trying again with a more adequate dosage. The massive dose would certainly get over the question of dose frequency, and he knew of no objection to it.

The essential surgical principle should be preserved—where there was pus it should be let out. The maintenance of the patency of the eustachian tube was important, and here he desired to mention the experience he had had during six years of war in the Services. He had found the use of ephedrine-saline, either as spray or drops—preferably drops—in the head-hanging position, combined with the administration of alkalis by mouth, as helping to re-establish the patency of the eustachian tube in a great many cases. He knew there were objections to the alkali method, but in actual working out it did prove effective.

The other point concerned the return to normal hearing. In the treatment of these cases by inadequate doses of sulphonamides, granulations formed in the middle ear. This had been found in other fields, e.g. in quinsies, where sulphonamide dosage had been inadequate, granulation tissue formation was excessive. While the acute symptoms in

It seems quite clear that the hæmolytic streptococci respond most quickly and the pneumococci least quickly while cases with secondary infections are very resistant. This again would conform to our previous impressions.

The most interesting fact which emerges from these figures is that the average dose required in Group A, 2,500,000 units, is larger than that used in all cases of strep. and staph. infections in both Groups B and C.

Results of treatment.—The two main criteria are (1) restoration of hearing, and (2) a dry ear. There are fortunately no deaths to record in this series. The mortality of this disease, particularly with regard to its serious complications, has undergone a marked change since the advent of the sulphonamides and penicillin.

From the point of view of the restoration of hearing it is difficult to assess the results as one feels that a not inconsiderable number of those cases in which the hearing remained impaired after treatment already had some hearing loss before the attack for which they were treated.

The actual results are as shown in Table IV.

TABLE IV.					
	No. of cases	Very poor	Impaired	No complaint or normal	Percentage with loss of hearing
Group A	18	—	1	17	6
Group B	50	2	7	41	18
Group C	42	2	14	26	38
Total	110	4	22	84	24
Simple infection	90	2	14	74	17.8
Sec. organisms present	20	2	8	10	50
20,000 units	23	2	6	15	55
60,000 units	87	2	14	71	18

It is fair to assume that the majority of these cases showing secondary organisms had some impairment of hearing before treatment and if these cases were removed from the list there remains hearing loss in 16 cases out of 90 or 17.8%. Out of the 23 treated with the smaller doses 8 had some impairment of hearing, 35%, while with the larger doses the % is 18.

Table V shows continuance of discharge.

TABLE V.—DISCHARGE.				
		Discharge	Dry	Percentage with discharge
All cases	110	5	102	7
Simple infections	90	1	89	1
Sec. organisms	20	7	13	35
20,000	23	5	18	22
60,000	87	3	84	3

This continued in 8 cases while in 102 a dry ear resulted, that is roughly 7%. Seven of these cases were those with secondary organisms present while the other case was originally a staphylococcus four times resistant. Two of the cases with moist ears were associated with traumatic perforations, one of which had previously been treated with drops and the other occurred while swimming. Five of the cases had the smaller dose while three had 60,000 units. These are the bare figures and the most difficult part of my task is to decide what conclusions can reasonably be drawn from them.

In the first place one cannot but help noticing the difference in the results of treatment by doses of 20,000 units per injection as compared with higher doses.

For hearing results the comparative figures of hearing loss are 35% as compared with 18%, while for persistent discharge they are 22% as compared with 3%. These results are ample confirmation of the wisdom of using the increased dosage.

I regret that I cannot give any useful statistics of the comparative results of those cases treated with and without sulphonamides. Unfortunately, many of them were treated—often with inadequate doses—before coming under our care so that comparison would be misleading.

This is a pity because there have been reports recently of acute infections treated by a combination of penicillin and sulphonamides in which the results of the combined treatment are of a very satisfactory nature.

In the next place I think some significance attaches to the figures of dosage in Group A. Obviously no hard and fast rules can be laid down in any particular case and our practice has been to carry on with treatment until the congestion of the drum has subsided and the landmarks are again clearly established. This has meant that treatment has gone on for five or six days as an average in this group. This dosage may perhaps

Section of Laryngology with Section of Otology

COMBINED SUMMER MEETING HELD IN TORQUAY

[June 14, 1946]

LARYNGOLOGICAL SESSION

Chairman—G. EWART MARTIN, F.R.C.S.Ed.

(President of the Section of Laryngology)

The Application of Electromyography to Affections of the Facial and the Intrinsic Laryngeal Muscles

By B. FEINSTEIN.

ELECTROMYOGRAPHY is a delicate gauge of the damage to the lower motor neuron and it has proved of value for the accurate assessment of peripheral nerve injuries and the early stages of diseases affecting the lower motor neuron. Among other pathological conditions, it has been an aid in the diagnosis and prognosis of facial and laryngeal muscle affections (Weddell, Feinstein and Pattle, 1944). Muscles which perform finely graded movements such as those of the face and larynx have motor units composed of fewer muscle fibres than those muscles, such as of the limb, which are only capable of much coarser movements. The action potentials are similarly less in duration (2 to 5 milliseconds) and smaller in amplitude (50 to 500 microvolts).

Facial paralysis.—Electromyographic examinations have been carried out in more than 150 cases of facial paralysis due to affection of the lower motor neuron. The cause of the paralysis, in the majority of the cases, can be divided into two clearly defined groups.

In the first group, the paralysis is due to trauma, either direct or indirect, and in the second, the paralysis is due to pressure by inflammatory oedema on the nerve trunk in its course through the temporal bone, resulting in an ischemic block. In this group can be included the paralysis found in such conditions as Bell's palsy, herpes zoster and otitis media.

It has been found that the facial paralysis following a head injury in the majority of cases is apparently due to an ischemic block rather than to an interruption of the axons. This would account for the observations of Turner (1944) that the prognosis in facial paralysis of this type is good. 12 cases of traumatic facial paralysis were examined electromyographically. In 4 of these, there was no evidence of denervation and each made a complete recovery, but, in each of the other cases, there was a varying number of axons interrupted. Recovery occurred but associated movements were present in every instance.

The findings suggest that in cases of complete axonal interruption following direct trauma, where there is no gross displacement of the nerve, at least six months should elapse before operative procedures, such as exploration and grafting, are to be considered. In such cases electromyographic examinations are valuable in detecting minimal degrees of re-innervation before the return of functional recovery. In those cases where the skiagrams demonstrate a fracture and displacement of the mastoid tip, earlier operation is justified. In cases of closed head injuries, the prognosis regarding the recovery of facial paralysis is so good that early decompression of the facial nerve is not warranted.

the ear subsided, deafness remained, due to the contraction of the granulation tissue. He wondered whether something similar happened in ears where the dosage of penicillin was inadequate.

Mr. G. H. Bateman said that Group A bothered him very considerably. It was almost impossible to estimate whether to leave the condition alone or not in these cases, and any figures produced for Group A seemed to him rather in the realm of guesswork. Perhaps Mr. Wilson would define a little more clearly whether he had referred to cases in which suppuration had occurred or cases in which he thought it might occur.

Mr. H. V. Forster said that he was grateful that this point had been brought forward by Mr. Wilson and Mr. Bateman. Mr. Wilson had stated that these were cases of potentially acute suppurative otitis media.

He, Mr. Forster, had always disliked the academic distinction made between acute catarrhal and acute suppurative otitis media when it was meant to imply that the former was a less severe type of the same disease.

The term, acute catarrhal, might lead to confusion in our conception of exudative catarrhal otitis media or "secretory otitis media" (see Eagle, Watt W. (1946) *Annals Otol. Rhino., Laryng.*, St. Louis, M.O., U.S.A., 55, 55).

Mr. Gavin Livingstone spoke of cases of mastoiditis in which much smaller doses than those mentioned by Mr. Wilson had been given, namely, 20,000 units of penicillin. There had been no surgical interference. Out of 16 cases there had been five failures; the others had cleared up entirely. In the cases which were failures there was no adequate drainage. In two cases the middle ear was not draining at all. The conclusion was that penicillin was of no use unless drainage was taking place through the middle ear. Future cases might be tried on larger doses.

Mr. C. P. Wilson, in reply, said that he was neither advocating nor defending penicillin. He was not suggesting that he would ever treat another group such as the A group. He started treating the A group four months ago when he was first asked if he would take part in this discussion, and it was solely to see what information he might obtain by treating these cases that he did so. They were cases which, if left, would have become cases of acute suppurative otitis media. The difficulty in those cases with definite mastoiditis lay in telling beforehand that they were of a type which would not respond completely to penicillin. Failure might be associated with the size of the individual cell; there might be so much pus in the cells that the penicillin did not get into them. It might be possible to get a clue by X-ray picture of the anatomy of the cell distribution.

He thoroughly agreed as to the importance of early puncture of the drum; all cases should have a myringotomy done at an early opportunity. The treatment for acute suppurative otitis or acute otitis media that might be suppurative was really still myringotomy. So far as dosage with penicillin was concerned, no difference was made in this series with regard to age; it was the same for the infant as for the adult. Local penicillin was not used in any of these cases.

Electromyographic examination has been found to be of value in cases of "idiopathic laryngeal palsy". In a few of these cases, normal motor unit activity was obtained from the muscles which were thought to be affected, and the immobility of the cords was shown to be due to ankylosis of the arytenoid cartilage. A certain degree of recovery in these cases is possible by re-education. Vocal cord paralysis as a result of denervation of the intrinsic laryngeal muscles was diagnosed by the presence of fibrillation action potentials. In these cases, recovery was not so good although it was possible at times to pick up polyphasic motor unit action potentials indicative of re-innervation.

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R. G. Macbeth described electromyography of the laryngeal muscles, first giving the technique and then proceeding to some illustrative cases. The patient was premedicated and prepared with surface anaesthesia as for any direct laryngoscopy, and the larynx was examined by the ordinary routine. Any diagnostic laryngoscope might be employed. Usually the crico-arytenoideus lateralis muscle was initially explored, on the unaffected side first and then on the affected side. Then the posticus muscles were similarly explored. The lateralis muscle was reached by inserting the bipolar electrode through the aryepiglottic fold lateral to the cord. The posticus muscle was reached by passing the beak of the laryngoscope behind the arytenoids to each side of the mid-line in turn and inserting the electrode 1 to 2 cm. below the level towards the back of the cricoid cartilage. The patient was instructed to phonate or breathe deeply as required. By this technique doubtful cases of paralysis, crico-arytenoid fixation, and hysterical aphonia might be diagnosed with reasonable certainty. No untoward effects of the examination, except slight soreness, had been noted to date.

Mr. Macbeth then mentioned three illustrative cases:

(1) A lieutenant in the U.S. Army Air Corps was hit in the neck by a piece of flak. This had entered anteriorly on the right side and come to rest in the posterior muscles. He had become hoarse immediately after being struck, and remained so. Laryngoscopy showed the right cord immobile in the cadaveric position. Electromyography one month later revealed complete axonal interruption of the recurrent nerve on that side.

(2) A sergeant in the same Corps was hit in the neck near the larynx on the right side by flak. There was a history of considerable swelling in the region of the thyroid cartilage, which had subsided, and of hoarseness, which had persisted. Laryngoscopy two months later showed the right cord fixed in abduction and some thickening of the aryteno-epiglottic fold. Electromyography showed intact innervation on the affected side. Crico-arytenoid ankylosis, already suspected clinically, was thus confirmed.

(3) A Guardsman was undergoing preliminary training when he fell upon a tree-trunk and badly bruised the right side of his neck. There was considerable swelling, which subsided, and hoarseness, which persisted for six months. He had been discharged from the Army with a diagnosis of recurrent laryngeal nerve paralysis, after having been examined by a number of otolaryngologists. When seen in civilian life the right cord was in the cadaveric position and nothing else was to be made out clinically. X-rays of the laryngeal cartilage showed no fracture. Electromyography of the laryngeal musculature showed full motor activity on the affected side. His discharge diagnosis was thus disproved, and it became clear that he had a fixation of the crico-arytenoid joint.

A New Œsophagoscope

Martin Henry said that the distally illuminated œsophagoscope of the tubular type gave admirable illumination at the position where it was most needed, but it was difficult to manipulate, and being necessarily of the tubular pattern the field of view was restricted. The disadvantage of the proximally illuminated type of instrument was that, while giving an admirable open field at the end of the scope, it had diminished illumination.

He had designed an œsophagoscope which gave an open field of view at the distal end, was easy to manipulate, and afforded adequate illumination. A definite improvement in the illumination of proximally illuminated instruments could be obtained by aligning the lamps so that they bore directly on the distal end of the instrument. Existing instruments carrying their lights in long tubes were focused on the walls of the main tube, the illumination finally reaching the tip of the œsophagoscope by means of cross reflection, so that a proportion of the illuminating power of each bulb was lost. In his instrument the lamp-carrying tubes, instead of being some inches long, were only just long enough to prevent reflection from the bulb reaching the surgeon's eye. In this instrument the lamp-carrying tubes were inside the œsophagoscope. If the instrument was examined without the lamp-carrying saddle in it it would be noted that whether

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The demonstration of even a single repetitive motor unit action potential is of great prognostic significance in a case in which clinically the paralysis is complete, as it indicates that a few nerve fibres have escaped damage, and therefore suggests that the lesion is "in continuity".

In the cases of the infective group, i.e. Bell's palsy, herpes zoster and otitis media, electromyographic examinations confirm the clinical observations, but, in addition, offer a more detailed analysis of the nature of the paralysis. This is particularly valuable in assessing the prognosis. In mild cases of facial paresis, there was a reduction of motor unit activity in response to a maximum voluntary effort to move the muscles but no other abnormalities. Recovery both clinically and as shown by means of electromyographic recordings was complete within a few weeks. In instances where the facial weakness was more marked and associated with a considerable degree of lower motor neuron denervation, recovery resulted in marked associated movements. This is accounted for by the fact that many of the regenerating axons do not follow their original pathways and dichotomization of the axon is frequent. The work of Howe, Tower and Duel (1937) has placed the phenomenon of associated movement following re-innervation on an anatomical basis, and the ultimate prognosis regarding the dissociated movement of the facial muscles is poor in view of this abnormal pattern of innervation. It may be possible, however, in some instances to improve the degree of recovery. Two cases of facial paralysis, in which there was complete axonal interruption, were followed through to functional recovery and their treatment carefully controlled. They were started on a daily session of "galvanism" and were also shown how to massage their faces, which they did a number of times daily. In addition, the angle of the mouth was kept elevated by means of a "facial" hook. Electromyographic recordings were made at weekly intervals and soon after the appearance of the first motor unit action potentials slight movement was observed on attempted voluntary contraction. The "galvanism" was then stopped and the patient began to practise individual facial movements in front of a mirror every day. The mode of regeneration and basis of associated movements were explained to the patients. In both instances, the patients were co-operative and in both cases associated movements were less than was usually seen.

Ballance and Duel (1932) have advocated that the facial nerve should be decompressed immediately a facial paralysis is seen in order to prevent axonal interruption, but, in view of the work of Denny-Brown and Brenner (1944a and b), it does not seem likely that many operations could be carried out in time to be effective. Furthermore, it is doubtful, from the anatomical point of view, whether exposure of the facial nerve from the lateral semicircular canal to the stylomastoid foramen and incising its sheath, is an adequate decompression. Kettel (1943) analysed a large number of cases of facial paralysis, associated with otitis media or mastoid infection, but came to no definite conclusion as to the optimum time for operation. He was, however, of the opinion that, in cases of immediate complete facial paralysis following mastoidectomy or labyrinthectomy, the facial nerve should be explored within seventy-two hours. In these cases, the operation of decompression seems to be of theoretical rather than practical value.

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There were three cases of very long-standing paralysis in which there was marked contracture. The contracture was confirmed as being due to fibrous metaplasia, for there were numerous areas of electrical "silence" in the facial muscles when electromyographic examinations were made. These patients had received no physiotherapy.

The intrinsic laryngeal musculature.—In order to record the action potentials from the intrinsic muscles of the larynx, it was necessary to use a concentric needle electrode of sufficient length so that all manipulations could be carried out through a laryngoscope.

The intrinsic muscles of the larynx have been investigated in a number of cases. The motor unit action potentials resemble those obtained from the facial musculature. The needle was first inserted into the lateral crico-arytenoid muscles and the subject requested to abduct the cords by taking a deep breath. There was continuous motor activity as long as the cords were abducted. When the cords were adducted, the motor unit activity decreased but did not die away completely. Thus the abductor muscles, even when the cords are adducted, maintain a certain amount of "tone".

Electromyographic examination has been found to be of value in cases of "idiopathic laryngeal palsy". In a few of these cases, normal motor unit activity was obtained from the muscles which were thought to be affected, and the immobility of the cords was shown to be due to ankylosis of the arytenoid cartilage. A certain degree of recovery in these cases is possible by re-education. Vocal cord paralysis as a result of denervation of the intrinsic laryngeal muscles was diagnosed by the presence of fibrillation action potentials. In these cases, recovery was not so good although it was possible at times to pick up polyphasic motor unit action potentials indicative of re-innervation.

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R. G. Macbeth described electromyography of the laryngeal muscles, first giving the technique and then proceeding to some illustrative cases. The patient was premedicated and prepared with surface anæsthesia as for any direct laryngoscopy, and the larynx was examined by the ordinary routine. Any diagnostic laryngoscopy might be employed. Usually the crico-arytenoid lateral muscle was initially explored, on the unaffected side first and then on the affected side. Then the posticus muscles were similarly explored. The lateral muscle was reached by inserting the bipolar electrode through the aryepiglottic fold lateral to the cord. The posticus muscle was reached by passing the beak of the laryngoscope behind the arytenoids to each side of the mid-line in turn and inserting the electrode 1 to 2 cm. below the level towards the back of the cricoid cartilage. The patient was instructed to phonate or breathe deeply as required. By this technique doubtful cases of paralysis, crico-arytenoid fixation, and hysterical aphonia might be diagnosed with reasonable certainty. No untoward effects of the examination, except slight soreness, had been noted to date.

Mr. Macbeth then mentioned three illustrative cases:

(1) A lieutenant in the U.S. Army Air Corps was hit in the neck by a piece of flak. This had entered anteriorly on the right side and come to rest in the posterior muscles. He had become hoarse immediately after being struck, and remained so. Laryngoscopy showed the right cord immobile in the cadaveric position. Electromyography one month later revealed complete axonal interruption of the recurrent nerve on that side.

(2) A sergeant in the same Corps was hit in the neck near the larynx on the right side by flak. There was a history of considerable swelling in the region of the thyroid cartilage, which had subsided, and of hoarseness, which had persisted. Laryngoscopy two months later showed the right cord fixed in abduction and some thickening of the aryteno-epiglottic fold. Electromyography showed intact innervation on the affected side. Crico-arytenoid ankylosis, already suspected clinically, was thus confirmed.

(3) A Guardsman was undergoing preliminary training when he fell upon a tree-trunk and badly bruised the right side of his neck. There was considerable swelling, which subsided, and hoarseness, which persisted for six months. He had been discharged from the Army with a diagnosis of recurrent laryngeal nerve paralysis, after having been examined by a number of otolaryngologists. When seen in civilian life the right cord was in the cadaveric position and nothing else was to be made out clinically. X-rays of the laryngeal cartilage showed no fracture. Electromyography of the laryngeal musculature showed full motor activity on the affected side. His discharge diagnosis was thus proved, and it became clear that he had a fixation of the crico-arytenoid joint.

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The Chairman said that in Edinburgh they had a cancer research department of which the radiologist was in charge. In every case from the pathology department which was diagnosed as tumour, a report was sent direct to the cancer research department. If the growth was in the centre of the cord, extending slightly below, it was considered very much better to use radium, but if further back this was thought to be useless. Teleradium had been almost given up in favour of deep X-rays of heavy voltage, nearly up to one million. The fenestration operation gave a better voice result than the treatment of the cord by deep X-rays. When there was recurrence after the use of deep X-rays nothing could be done apart from attempting laryngofissure, but if radium needles had been used, deep X-rays could be used later on from the opposite side with suitable screening.

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Xanthoma of Upper Jaw.

Man, aged 39, ex-R.A.F. Admitted March 1946 with proptosis and failure of vision in right eye. X-rays showed opacity of right antrum. Exploration revealed a large encapsulated tumour expanding the antrum; this was removed. Severe hæmorrhage necessitated packing. There was still a fistula on discharge from hospital on May 1. Vision improved from 6/60 to 6/9, with disappearance of central scotoma and improvement of field. The fistula has now healed and the nose is normal.

W. H. Bradbeer said that this was one of those cases which looked formidable at first but ended happily. Xanthomata were not uncommon in the skull, especially in the petrous bone. Sometimes they were single, but there were multiple cases occurring especially in the long bones. In some cases there was also proptosis and disturbance of pituitary function, and the condition was known as the Hand-Schüller-Christian syndrome. One interesting point was that this condition tended to occur in jaundiced patients. This patient was suffering on admission from a sharp attack of benign tertian malaria, with a marked anaemia (Hb. 60%) so that it was possible he might have some hæmolytic jaundice in connexion with his xanthoma.

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Woman, aged 63. Treated since April 1945 for extensive blastomycotic lesions of skin. Great improvement following X-rays, potassium iodide and gold treatment. Nose shows small perforation of septum and granular condition of inferior turbinals from which the *Blastomyces dermatitidis* has, on one occasion, been identified.

H. W. Allen (Exeter) said that this was one of the first cases of the American type described in this country. The patient was first seen by him in April 1945, complaining of skin trouble affecting the cheeks and nose for a year. There were a number of minor complaints—chilblains, &c. Two or three years previously she had laryngitis. The present skin trouble started as a rash under the skin, later forming a crust; when the crust came off, a red patch was exposed and pus could be expressed. Microscopic examination of the pus showed typical blastomycetic mycelium and yeast-like double-contoured cells, which he thought he confirmed by culture. [He showed two cultures which had been obtained from the case shown and from another case of ulcerative blastomycosis; the latter had been reported on as a blastomycosis, but this appeared to him to be questionable: the former was considered to show a fairly typical colony of *Blastomyces dermatitidis* with abruptly rising edge and eccentric areola.] There was no question of residence abroad in this case, and the only suggestion that this could be American blastomycosis came from the fact that American negro troops had been in the

the observer looked through the lumen of the main tube or down either of the empty lamp-carrying tubes a complete view of the field afforded by the tip of the instrument was obtained.

He had had these instruments made in very much larger sizes than usual, first because the larger the instrument the easier it was to find the way into the œsophagoscope, and secondly because the chief limitation to the size of the œsophagoscope was not the size of the œsophagus, which was enormously dilatable, but the anteroposterior space between the upper and lower teeth. One of these models was built for edentulous adults and in spite of its large size would pass freely down the œsophagus of any edentulous adult without inflicting any trauma.

These œsophagoscopes were made in the following sizes: 30 cm. for children; 40 and 30 cm., medium adult; 40 and 30 cm., large adult; 40 and 30 cm., edentulous adult.

[June 15, 1946]

CLINICAL MEETING AT TORBAY HOSPITAL

Chairman—G. EWART MARTIN, F.R.C.S.Ed.

(President of the Section of Laryngology)

X-ray Films of Radium Needles *in situ* following Fenestration Operation.

The operation was performed by Mr. Negus and Mr. Bradbeer in December 1941. Dosage 8,640 mg. hrs. Patient free from recurrence, but in September 1945 had an attack of perichondritis and coughed up a piece of cartilage.

V. E. Negus said that this was an elderly man who was considered unfit for an excision operation, with a growth which extended along one cord. The moral of the case was that there was a use for the application of radium to the larynx. It seemed to him that radium was more logical than radon. Deep X-ray treatment for the larynx he thought to have disadvantages, and it was upsetting to the patient. Teleradium with a 5-gramme unit was less so, but many patients complained during the treatment and some wanted to stop it. It took four to five weeks, whereas the application of radium needles might be over in about seven days. The previous week he had seen a patient who had had the larynx irradiated by teleradium four years ago and had had a mild perichondritis ever since. This did not seem to occur so much with needles. The present patient had been perfectly well for some years, and then this attack of perichondritis developed four years after the operation. He could not think that Mr. Harmer's recommendation to use radium needles should be put aside without due thought; there seemed to be certain conditions in which it might be a very suitable form of treatment.

The Chairman said that he had had two cases in which the condition had apparently cleared up, and after eighteen months or two years perichondritis had developed on the other side.

V. E. Negus said that the dosage might have been a little higher than necessary. Harmer now recommended four vertical and two horizontal needles—a total of 10 mg. for seven days. He thought the way to avoid perichondritis developing on the opposite side was to ensure that the foremost needle was not too near to the cut edge of the thyroid ala.

J. C. Hogg said that he had assisted Mr. Douglas Harmer in a large number of these cases and could vouch that they did extremely well on the average. The actual screenage was extremely important, if the development of perichondritis immediately or subsequently was to be avoided. Mr. Harmer had originally employed 0.5 mm. platinum filter, but he went rapidly to 0.6 and now never employed anything less than 0.8, and with this he had had far less trouble with post-operative sepsis and subsequent perichondritis. In fact, he had not had perichondritis due to this operation for some time now.

On the question of a horizontal or vertical palisade, a team of physicists at Mount Vernon produced a paper on the physics of the arrangement, showing just where the maximum dosage was received. He joined issue slightly with Mr. Negus as to the indications for this procedure. By and large, those cases which had a growth extending on to the arytenoid were not so favourable from the physical aspect. The intensity was not retained in that area owing to the depth of the growth from the needle, and therefore those cases had not relatively as good a prognosis as they would have with laryngectomy. On the other hand, it could be said quite definitely that cases which were limited to the middle third of the cord or the anterior commissure would obtain cure or relief as readily as the cases which had the cord removed, and with much better voices afterwards. There was no doubt that of the two elements, radon or radium, radium needles were far better. Mr. Harmer was unable for a short period at the beginning of the war to obtain radium needles and had to use radon for a time. In his opinion the radium needles were far better.

E. D. D. Davis said that one of the disadvantages of the use of radium implantation was that there was considerable suppuration and a puckered scar was left in the neck. For his own part, if he could not have a complete excision and if he had to have radium or deep X-rays, he would prefer X-ray therapy.

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neighbourhood where she had been staying. X-ray treatment of the face was advised, to which the skin responded readily. She responded to iodide and salicylates as well. In July 1945 the pulse-rate was 100 a minute, at which it still remained; she lost her slight pyrexia for a time, but relapses occur. The nasal condition was noted in October 1945; he thought there was a perforation of the septum. Gold treatment seemed to have improved her, or at any rate to have done her no harm. An X-ray photograph of the chest was also taken, but no complete evidence that the disease was spreading to involve the lungs had been obtained. The X-ray shows infiltration at left base as a light diffuse shadow. Mr. Bradbeer confirmed that cultures from nasal mucosa and skin were positive.

The Chairman said that he had seen three cases of blastomycosis of the chest. None of the physicians had heard of it, and in most of the recent books there was no mention of it. If he had seen this case without the history he would have said it was typical of lupus.

E. D. D. Davis said that he thought this was a case of lupus. There was a lacrimal sac infection, and there were scars on the tip of the nose and of a gland excision in the neck.

Non-malignant Stricture of Oesophagus.

Woman aged 29. History of difficulty in swallowing for about three months. Was said to have swallowed some potassium permanganate crystals. X-ray showed obstruction in upper third of oesophagus. Wassermann reaction negative. Oesophagoscopy revealed a stricture which has been dilated three times with only temporary improvement.

W. H. Bradbeer showed this case for information.

V. E. Negus said that in the treatment of this case a large oesophagoscope was required. It was important to see what the surface was like, whether the epithelium were denuded or not. Generally speaking, the result ought to be good with simple dilatation. There was a great difference in the way it was done. If bougies were put through a tight stricture one was likely to strip the epithelium. He used the dilating bag which slipped down a guide, and this bag when blown up would dilate to the size of four fingers. Possibly the stricture would have to be dilated every six months. In a small boy aged 1½ years, in whom the X-rays were identical with those in the case now shown, and in whom there was an under-development of the oesophagus at this point, as there was in congenital shortening, with lack of proper covering by epithelium, he had tried to improve matters by applying a skin graft, by making a little bag in a dumb-bell manner which could be blown up with a graft on it. He would have said that in a case like the one shown there was no radical treatment possible. Anastomosis would prove to be unsatisfactory.

Ian Robin asked how tight was the stricture.

W. H. Bradbeer said that it dilated very easily. He had dilated three times in two months and the patient only improved for a short period.

Ian Robin suggested that the patient might be instructed to pass a mercury bougie herself daily. He had a similar case which he had to dilate with olive bougies on a string, and then the patient was quite comfortable passing the mercury one, at first before every meal and now once a week.

A. J. Wright said that a good deal depended on the stage of the stricture. If there was recent injury of the oesophagus, provided the patient could be kept in a reasonable state of nutrition, the wise thing would be to leave it alone for six months or so. Interference in the acute stage of any oesophageal lesion tended to make matters worse rather than better. But it was rather difficult to say whether this was recent or not.

The Chairman said that he hoped to show the results in four cases seen in children who had traumatic strictures following the swallowing of sulphuric acid or something of that kind. The oesophagoscope had been used and a dilator passed through to determine the consistency of the stricture and then a gastrostomy had been done. The curious thing was that all these children who were able to carry on at school with a gastrostomy tube would have an ounce of milk given by the gastrostomy tube in the morning and this set up a reverse peristalsis which actually dilated the stricture, so that they could be given a soft meal, almost an ordinary meal, by the mouth in the afternoon. Two of these cases were now fit radiologically and accepted an ordinary sized oesophagoscope. The other two had so much improved that he thought the gastrostomy tube would be removed quite soon.

Section of Pathology

President—Professor W. G. BARNARD, F.R.C.P.

[July 2, 1946]

ADDRESSES GIVEN AT THE CENTENARY CELEBRATIONS OF THE PATHOLOGICAL
SOCIETY OF LONDON

The Pathological Society of London

By Professor H. R. DEAN

It is my first duty to thank you for the honour which you to-day have done to the still surviving members of the Pathological Society of London. You have asked me to tell you about the early days of the Society, but one hundred years is a long time and I can do no better than read to you extracts from the early volumes of our *Transactions* and let our predecessors speak to you in their own words.

"The establishment of a Society which should devote itself specially to the cultivation of Pathology, and render more generally available for this purpose the extensive opportunities afforded by the numerous Medical Charities of the Metropolis, had long appeared to several Members of the Profession to be desirable."

"In February 1846 several gentlemen met together and agreed upon the issue of a circular to such Members of the Profession as were known to be more particularly interested in Pathological Studies."

"A Provisional Committee of Gentlemen who had expressed their concurrence was appointed and agreed upon the issue of a Prospectus to the Members of the Profession at large, inviting their support and co-operation." This appeal met with unexpected support and on October 20, 1846, at the first Meeting of the Society there were enrolled one hundred and six members. C. J. B. Williams, M.D., F.R.S., was appointed President and B. G. Babington, M.D., F.R.S., Richard Bright, M.D., F.R.S., J. Glendinning, M.D., F.R.S., John Forbes, M.D., F.R.S., J. M. Arnott, F.R.S., Caesar Hawkins, C. A. Key, Robert Liston, F.R.S., were appointed Vice-Presidents and James Copland, M.D., F.R.S., was appointed Treasurer.

The President, the Treasurer and six Vice-Presidents were Fellows of the Royal Society and the Council "conceived that their names were too well known to the Profession to require any comment on their part, and they could not but congratulate the Society upon having secured the countenance and services of gentlemen whose high position and

distinguished attainments offered a sure guarantee for the support the Society would receive at their hands".

Among the original members were Richard Bright, Golding Bird, William Gull, William Jenner, Bence-Jones, Henry Pavey, Richard Quain and John Queckett. The first list of Honorary Members included J. C. Cruveilhier, William Stokes and C. Rokitsansky.

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In the later fifties well-known names appear frequently in the pages of the *Transactions*. Murchison, Spencer Wells, Samuel Wilks, Christopher Heath, Bristowe and Thomas Bryant showed many specimens to the Society. In 1861 Thomas Nunneley of Leeds reported a case of rupture of a gangrenous appendix followed by peritonitis and in December of that year Jonathan Hutchinson described to the Society syphilitic ulceration of the bones of the skull with deposits on their inner surfaces: "At two points, one on the posterior half of the right parietal bone and the other on the left side of the frontal bone, were deposits of new bone, much resembling sawdust stained with blood, about as large as a crown piece."

In its first decade our Society encouraged the study of morbid anatomy rather than of morbid processes. "Our Founders had also the wisdom", as John Whitaker Hulke declared in his Presidential Address, "to recognize that no durable theory, no sufficient explanation of the processes causing structural derangement could be formed except on the solid basis of facts. The accumulation of facts was to be the Society's first care".

The foundation of our Society followed very closely upon the great discoveries then so recently made in normal histology or as it was then called "general anatomy" through "the improvement of the microscope and by the employment of methods before unknown or little used, particularly the preparation of finer and more transparent sections made possible by chemically hardening the tissues and by their differential staining".

The publication in 1858 of Virchow's lectures on cellular pathology, followed five years later by his book on the pathogenic tumours, opened a new chapter in the history of our Society. As a President of the Society remarked: "Yet, with a full appreciation of the paramount importance of established well-ascertained facts, inferences could not be altogether avoided; they would frequently force themselves upon the observer and out of them theories would sometimes arise. Who, having observed the clinical phenomena of inflammation, could avoid speculating as to its essential nature and its causes? Who familiar with the clinical courses of a cancer and a fibrous tumour and possessing some knowledge of histology could avoid the interesting question—What is it which confers on the one the endowments which we sum up under the word malignant, and gives to the other those implied by the term innocent?"

In 1869 four years after the publication of "*Die Krankhaften Geschwülste*" the Society set up a "Committee on Morbid Growths and Processes" in order "to ascertain if any and what relation exists between anatomical structure and those clinical features ordinarily regarded as malignant".

Reports on specimens from isolated cases, however, continued to constitute the chief business of the Society and in the sixties there appear in the *Transactions* names of men destined to play a great part in the development of the Medical Sciences. In 1863 Burdon Sanderson demonstrated sections of a fibro-cellular tumour of the ureter and Broadbent described a malignant tumour of the occipital bone. In 1864 Morell Mackenzie gave the first of a series of reports of tumours of the larynx and in the following year Hilton Fagge described "bronchial casts in asthma containing numerous bright rounded particles which appeared to myself and Dr. Wilks to be shrivelled nuclei".

Comparative pathology was not neglected. In 1848 Mr. Crisp exhibited six specimens illustrating disease in the lower animals including "the testicle of a ram converted into calcareous matter" and "a fungoid tumour from the eye of a canary". Other specimens exhibited to the Society were the spleen of a bull that died of splenic apoplexy, enlarged thyroid glands in young lions, diseased renal bodies in a camel, and "the colon of a sheep showing colotomy performed by a parrot".

In 1882 the Society appointed a standing Committee for Comparative Pathology and in 1887 there were communications on the diseases of vegetables.

Villemin's great discovery first published in 1865 that tuberculosis was a specific infection due to a then invisible inoculable agent transmissible from men to lower animals produced a quick response from members of the Society. In 1867 John Simon demonstrated the results of the inoculation of guinea-pigs and rabbits with material obtained from tuberculous patients and in the same year Burdon Sanderson found that the microscopical changes produced in animals by the introduction of tuberculous matter resembled closely the changes produced by sterile foreign bodies such as setons. From these experiments Sanderson drew the conclusion that the microscopical changes seen in tuberculosis were produced by the irritation of foreign bodies and that it was unnecessary to assume the existence of a living and infective virus. Three years later, however, as the result of an extensive series of experiments Sanderson was able to confirm Villemin's views by the demonstration of the close similarity of the lesions produced in experimentally infected animals with those found in the organs of tuberculous patients.

A great discussion was held under the auspices of the Society in April 1875 on the Germ Theory of Disease and it would be impossible to give here and now a summary of the arguments, for and against, put forward by Charlton Bastian, Burdon Sanderson, Jonathan Hutchinson, Murchison and other speakers. Although this discussion, carried through with great vigour on both sides, was inconclusive, communications on bacteriology became more frequent during the seventies, and in 1884 the President of the Society observed that "if all that has lately been written about these low forms of plant life be true, they would appear to take an active causative share in nearly all the ills to which flesh and blood are heir". The President added "the pages of our *Proceedings* show that our members have not been idlers in this branch of research".

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On June 4, 1907, the Pathological Society was dissolved and Samuel George Shattock wrote:

"Dissoluta est jam de die quarto Junii, 1907, Societas Pathologica Londinensis, Facultas ut fieret Pathologica Societatis regiae Medicinæ, in Londino nuper constitutæ. Quæcunque ad hanc Facultatem pertinent litteræ, conjunctim cum illis Societatis regiae Medicinæ abhinc in lucem edentur."

Cellular Pathology

By Professor G. R. CAMERON

By a strange coincidence, the life of our Society corresponds almost exactly with the rise of cellular theory, and cellular pathology in particular. Improvements in the production of microscopes made steady progress during the early years of the nineteenth century, and, in 1807, Van Deyl invented a compound microscope with achromatic objective, giving a magnification of 229. In the 1840's, large-scale microscope manufacture was going on on the Continent, and the fitting of microscopes with aplanatic and achromatic systems was a common affair. The finer structure of animal and plant life had been studied mostly by botanists throughout this period, and culminated in 1838 in the publications of Schleiden and Schwann, who gave us the famous generalization of the identity of animal and plant units of life. In the decade immediately before the foundation of our Society, the important fact was recognized that cells reproduce by direct division, though the nature of this process was not grasped until the 1870's when karyokinesis was fully worked out.

The next few years brought the discovery by Oscar Hertwig (1875) of the fusion of male and female gametes and an exact appreciation of the function of the nucleus. In this latter fundamental advance, the experimental cytologists, especially Nussbaum and Verworn, played a vital part.

From the 1890's onwards came the rediscovery of the Mendelian phenomena of heredity and their interpretation in terms of nuclear, especially chromosome, behaviour. During this period, too, the methods of physical and enzyme chemistry were applied to problems of the cell, in particular the discoveries by van't Hoff and Arrhenius, about the properties of solutions and electrolytic dissociation, whilst the elucidation of catalysis and fermentation by Berzelius and Ostwald revolutionized our notions of cell function. Long before this time, however, Graham (1861), in founding colloid science, laid the way open for a new attack on living matter. Some sort of an idea about this substance had been in existence for many years. The pioneer proto-zoologists of the eighteenth century no doubt were familiar with its cruder characteristics. Attempts at a more precise definition were made by Gruithuisen in 1811, Dujardin (1835), Purkinje (1837) and von Mohl (1846). To Purkinje we owe the term "protoplasm", the introduction of methods of fixation and staining and even a rudimentary microtome. The true place of protoplasm in the study of life was exactly stated by Max Schultze (1861) in his simplified definition of the cell as a mass of protoplasm containing a nucleus, and about the same time a broad view of the organism as a cell state was suggested by Rudolph Virchow (1858) and Brücke (1861). Whether the cell is the only living substance has since been disputed, hence it is better to speak of "cellular theory". Most biologists agree that intercellular substances and fibrils are non-living derivatives of protoplasm. Amongst such advocates was Lionel Beale, in his day a prominent member of our Society.

Shortly before the Pathological Society of London was founded in 1846, there appeared in 1845 a remarkable little book by John Goodsir and his brother, entitled "Anatomical and Pathological Observations", in which are set out some ideas about the relationship between cells and nutrition, and their importance in some pathological processes. John Goodsir clearly recognized the existence of cell territories in the organism. In this way he forestalled the better-known work of Rudolph Virchow, and it may rightly be claimed that he was one of the pioneers of cellular pathology. There is little doubt, however, that cellular pathology first came into its own with the publication in 1858 of Rudolph Virchow's "Die Cellular Pathologie". I believe Virchow's greatest contributions may be summarized as follows: Cells are the units of life and disease. They are grouped together to form territories under the control of blood-vessels. Unhealthy cells are unable to attract nutriment from their associated blood-vessels, and when this occurs, noxious ingredients pass to the blood, producing dyscrasias and metastatic disease. All disease-producing agents,

suppuration with infection. Morbid histology had supplemented morbid anatomy and morbid physiology was stimulated by the still newer science of bacteriology.

Mr. Hulke in an address to the Society pointed out that:

"The doctrine of diapedesis, the partial truth of which no unprejudiced observer can, I think, doubt, if held to the complete exclusion of all others, has never appeared to me to be free from serious difficulties. Of these I would instance three: the inconceivable numbers and rapidity in which the white blood-corpuscles must be formed in cases of extensive inflammations; the great obstacles they must have overcome in some of their wanderings to reach such resting-places in which they are sometimes found; and the singular change of endowments which the white blood-corpuscle sometimes undergoes in becoming a pus-corpuscle. In illustration of the first of these difficulties, let me instance the histological phenomena of erysipelas. Here the whole subcutaneous areolar tissue of a limb will in a few hours become stuffed with leucocytes, for the enumeration of which billions were too small a unit. How difficult is the conception that the formation of white blood-corpuscles could have been so augmented and accelerated as to have, in addition to the normal physiological requirements, supplied these countless swarms of emigrants. Other instances of such wonderful journeys might be cited, but those which I have adduced may suffice to show that implicit credence in travellers' tales is not always easy. Why the white blood-corpuscle, become pus-corpuscle, should lose its pristine innocence, and acquire so virulent a nature, as we know it sometimes has, may find its explanation in the observation made by Hueter, that the corpuscles of septic pus contain within them Schizomycetes.

"During the whole existence of our Society no theory has arisen that in its practical bearings can rank in importance with one which in the present decade has gained so many adherents. I mean the doctrine which teaches that the inception and maintenance of the inflammatory process are due to the influence of those living agents which appear to be inseparably connected with the process of putrefaction—a doctrine which has here been so ably expounded by Sir Joseph Lister, and which one of its ablest and most thoroughgoing continental advocates, the late Professor Hueter, whose early death all must deplore, embodied in the aphorism, 'Without Schizomycetes no sepsis—without sepsis no inflammation'."

In conclusion I cannot do better than quote a few sentences from the Presidential Address of Samuel Wilks delivered on February 19, 1881:

"I have always considered that the glory of this Society has lain in its cultivation of morbid anatomy. If this were not so, wherefore the need of its existence? Before its foundation other Societies were in full force, one of their functions being the discussion of questions of pathology, and to them the right still remains; but the opportunity was needed by which those engaged in the new science of pathology could organize their work and bring together facts, so as to place on a surer foundation the more substantial and material data on which so many morbid processes depend."

"Why so great devotion to pathology? Does it help us to cure the sick? Can it assist us in alleviating the sufferings of our fellow-creatures, which is the great object of our calling? Or, does not pathology keep far in advance of therapeutics? For my part I have not the slightest feeling of sympathy with these questions, for I believe that discoveries in pathology and therapeutics always go hand in hand. Of course, I know there is a doctrine which maintains that therapeutics has a basis on its own, and physiology and pathology may be altogether ignored. I need not remind you, gentlemen, who are engaged in scientific work, that such considerations as ulterior and practical results are not worthy of you. A scientific man is a worker for truth, and, in my experience, if he sees any other object before him than the immediate result of his investigations, or if he be working by any other light than the 'siccum lumen', of which Bacon speaks, he will miss his mark. The discovery of a new fact must bring with it good, although the scientific man works for truth alone, and feels that knowledge is its own reward."

"It would, indeed, be easy to show the enormous accumulation of knowledge which has arisen from a simple inspection of the dead, and we are proud to think that much of this is contained in our *Transactions*."

"In conclusion, let me say that our Society stands out prominently in the history of medicine as having taken a large share in the cultivation of one of its most important branches. It has made constant progress, and has never slackened in its work, and if you now, gentlemen, maintain it in the same path during my two years of office I shall be more than content."

Cellular pathology originated from the general study of the nature and origin of living things. Its future lies in maintaining this close connexion and fundamental advances will come only so long as this relation is preserved.

Chemical Pathology

By Professor E. C. DODDS

THE growth of chemical pathology has been characterized by great irregularity right from its inception. When systematic organic chemistry had been placed on a firm foundation by the organic chemists of the early part of the last century, almost without exception they worked on biological products. One only thinks of names of people like Liebig, Hoppe-Seyler and others to conjure up immediately the work on proteins, carbohydrates, hemoglobin, &c. There is no doubt that these men can be regarded as the originators of the interest in chemical pathology. By the middle of the last century, however, the growth of synthetic organic chemistry had developed, with the result that organic chemists of the day deserted the study of the natural products for the much more fascinating problems presented by this new science of organic chemistry.

By the end of the last century and the dawn of this one, chemical work in pathology was really confined to very elementary examination of the urine, fæces, gastric juices, &c., and the examination of the blood for chemical constituents was largely a research problem. No notable developments in the subject occurred in this country for a very long period due mainly to the lack of suitable methods. Very rapid developments were made in America, however, from 1912 onwards, when Folin began to publish the result of his researches on colorimetric methods. He realized that if a number of blood constituents were to be estimated, then some form of common filtrate must be prepared from a single specimen on which it would be possible to estimate urea, sugar, uric acid, non-protein nitrogen, &c. This he succeeded in doing by the introduction of the well-known tungstic acid method of precipitation. He developed colorimetric techniques for the estimation of practically every known constituent of blood. These methods were not used in this country until years after publication for three reasons: (1) The main developments were published during the 1914-1918 war when there were more urgent and immediate problems to attend to. (2) There existed a violent prejudice against colorimetric methods amongst British biological analysts. They regarded the colorimeter as a somewhat immoral instrument which enabled people to take a short cut to results which should only be arrived at by an elaborate technique performed by an expert. Finally, it must be admitted that there was a third reason, and that was the extraordinary inaccuracy of many of Folin's publications. Whilst he was a meticulous worker, he was an extremely careless writer, with the result that if one performed a method as he described it, the chances were that some untoward event would intervene such as a heavy precipitate or an unexplained colour which rendered the determination impossible. I remember myself struggling with a uric acid method in which, just before one made the colorimetric comparison, a dense white precipitate appeared, rendering comparison quite impossible. Unfortunately Folin was that type of genius who did not reply to letters. I always remember on my first visit to the States going to him and questioning him about this determination of uric acid. He replied imperturbably that he did not use that reagent at all now, and gave me an entirely different one that worked perfectly. By 1920, however, a number of people had struggled with Folin's methods and had actually got them to work and they are now the basis of the methods utilized in chemical pathology.

I would earnestly suggest that a greater number of posts be made for chemical pathologists in any future planning and that these posts should be independent, collaborating on terms of equality with the clinicians and the pathologists. To my mind it is a retrograde step to regard the chemical pathologist as an assistant to the pathologist because I am certain that if this attitude is persisted in, then the best type of biochemist will not be attracted to chemical pathology. Again I would like to suggest for consideration that the biochemist who takes up chemical pathology need not necessarily possess a medical qualification. It seems to me much more essential that he should have a first-class knowledge of chemistry and biochemistry and that he can leave the medical knowledge on the one hand to his clinical colleagues and on the other hand to his pathological colleagues.

except those which arise primarily in the blood, are derived from altered metabolism of cells. Cells are disturbed in a number of ways. Disturbed function, for instance, leads to exhaustion and fatigue; disturbed nutrition to hypertrophy, degeneration and inflammation; whilst if the formative function of cells be upset, there follows hyperplasia, pus formation, tuberculosis or neoplasms.

Virchow recognized the importance of the cell in inheritance, and his famous dictum "omnis cellula e cellula" is as important to genetics as it is to cellular theory in general. Virchow, however, was insistent that the discovery of causes of disease does not clear up the nature of such diseases. Throughout his long life, he returned to this idea and continually stressed the need for further information about the nature of protoplasm and its response to injury.

In this limited time I cannot do more than touch on a few problems which cellular pathology has elucidated. Amongst these of first importance is the question of inflammation. Blood cells were recognized soon after the invention of crude microscopes by Pisa (1656), Swammerdam (1658), Malpighi (1661-1665), Leeuwenhoek (1687). In 1824, the French biologist Dutrochet described the migration of white corpuscles through the walls of blood vessels, but he gave no reason for this. It remained for the British investigators, Augustus Waller and William Addison (1839-1846), to show that migration of white cells occurred from the vessels of an injured part, whilst, in 1850, Thomas Wharton Jones noted that granular leukocytes appeared in large number in wounds, moving out of the regional blood vessels by means of intrinsic movements. Wharton Jones described the margination of such corpuscles and he also studied the formation of fibrous tissue. The investigations of Julius Cohnheim crowded into an all too short life resulted in a dynamic idea of the process and gave us, with few exceptions, our modern views on inflammation. The controversies which sprang up around Cohnheim's work added much exact information about proliferation of tissue cells, including the tumour cell.

Closely related in time was the study of phagocytosis, and here again we note the important part played by the biologists. Virchow (1852) had seen red blood corpuscles inside other cells and had attributed this to mechanical pressure, a view which stultified the original observations of cellular pathologists for some years. Ernst Haeckel, in 1858, noted that indigo granules were taken up by amoeboid cells of gasteropods. About ten years later, von Recklinghausen, Ponfick and Langhans showed that carmine particles introduced into the circulation of animals were ingested by cells in the spleen, bone-marrow and liver, and indeed a few years before Preyer (1864) actually watched blood cells taking up particles. Robert Koch, in 1876, found anthrax bacilli in the round cells of frogs infected with that organism, and Grawitz, in 1879, described similar ingestion of a fungus from the lily of the valley. In an apparently forgotten observation, Roser, in 1881, suggested that immunity of plants and animals partly depends on the property of their contractile cells of ingesting micro-organisms, but it remained for Metchnikoff to establish the phagocytosis theory as we now know it.

It is thus possible to recognize three stages in the hundred years of cell theory and cellular pathology: (1) The pre-cellular period which overlaps into our period, when many of the fundamental observations about cells were made by isolated workers without any clear idea of a connecting link. (2) The cellular period, a stage of almost pure morphology with little emphasis on protoplasm. (3) A period of physico-chemical investigation, with more and more attention being given to the nature and function of protoplasm. Glimmerings of quantitative study appeared at this stage, which correspond with the rise of biochemistry and biophysics.

I believe we are now passing into a fourth stage, which might be called the "sub-microscopic period", in which as the result of the work of Astbury, Bernal, Schmitt and Schmidt, we are coming to think of protoplasm in terms of giant molecules and mono-molecular surface films and their physico-chemical properties, governed by molecular arrangements. This stage is progressing from a relatively simple colloid chemistry to the involved considerations of high polymer chemistry. For its development the most exacting requirements in scientific training will be necessary, for the methods of such special fields as polarization optics, X-ray crystallography and electron microscopy, together with an appreciation of the range of biology, would seem to be essential in the future training of the investigator into protoplasmic reactions.

At present, the only way out of this deadlock appears to be through the formation of teams comprising physicists, biologists and plant and animal pathologists. I doubt very much whether any of us could hope to cope with this type of research without a radical revision in our medical education.

the Middlesex Hospital. The method ultimately devised for obtaining large concentrates has now been adopted in America.

With these large concentrates which we prepared, Pollard was able to study the chemical nature of these viruses, showing that they contain phosphorus to such extent that they consist in a large part of nucleo-protein.

Filtration.—Another important step forward in the study of viruses of course was by ultra-filtration with specially prepared collodion membranes and I would like to draw attention to the important work in this respect which was carried out at the National Institute for Medical Research by Elford and others; with his series of gradocol membranes of different porosities he was able to determine actually the size of many viruses.

Growth.—The failure to grow viruses on ordinary medium was found to be due to the fact that viruses live and multiply inside the tissue cells and require to get their food by a parasitic process. As you all know this growth can now be promoted and watched in the allantoic cell of the growing chick embryo, a fact of great importance in the preparation of vaccines.

Vaccinia.—In dealing with individual virus infections it is right that the first place should be given to vaccinia on which so much work has been done in the early part of last century. Since then there has been great improvement in the preparation and purification of vaccinia virus and in this respect I must refer to Copeman who introduced the process of mixing the lymph with glycerine and then freezing to get rid of the contaminating bacteria, thus reducing to an almost infinitesimal point one of the most serious drawbacks to vaccination, the risk of secondary infection, and in the demonstration of elementary bodies in smallpox vaccine, the names of Mervyn Gordon and Ledingham must also be mentioned.

Another important discovery in this country with regard to vaccination was the recognition of post-vaccinal encephalitis in which Professor Turnbull and I worked in collaboration and definitely showed it to be a specific lesion of the central nervous system. In regard to other neurotropic viruses, I might mention here the studies carried out by Mervyn Gordon and others on the nature of this devastating disease of children, poliomyelitis. Much work was also done in the 1914-18 war on epidemic encephalitis by Marinesco, Hall, myself and others, when it was demonstrated to be of a virus nature—though other causes had been attributed, as for instance, a form of botulism, a rather amusing one, suggested by an old lady was that it was due to the bite of the bot fly!

Bacteriophages.—One of the most outstanding discoveries ever made in the virus field was made by a member of this Section, Professor Twort, who discovered the bacteriophage. Though much discussion has centred around the actual nature of the bacteriophage, the general opinion now is that it is a virus which is capable of living inside bacteria and destroying them. It is interesting to note that I was working in the same laboratory with Professor Twort at the London Hospital when he made his great discovery, and I was then able to follow the various stages of this discovery and to say that very early on he considered that it should be regarded as a virus. Twort's original paper contains all the essential features of this important and significant reaction. He observed that staphylococcal cultures obtained from vaccinia underwent a peculiar type of degenerative change due to the action of the bacteriophage. This simple observation has provided us with many new facts with regard to viruses, their size, function and behaviour and in addition has provided us with a means by which we can identify different strains of *Bact. typhosum*, staphylococci and other organisms. Though some still hold that this bacteriophage is really a self-catalytic breakdown, the general view is that bacteriophages are viruses and definitely particulate.

Influenza.—Up to the time of the last pandemic of influenza (1917-1918), the influenza bacillus of Pfeiffer held the field as the chief aetiological agent of epidemic influenza. But the failure to demonstrate regularly the presence of this organism in the catarrhal secretions in this pandemic of influenza raised some doubt as to its real aetiological significance. Following this, with the aim of demonstrating the presence of a virus, extensive researches were taken up in this country and in America, with the result that Laidlaw, Andrewes, and W. Smith were successful in demonstrating a filter-passing virus in certain cases of epidemic influenza and this work has been confirmed throughout the world and it has been shown that there is more than one strain of virus influenza and furthermore that the complete relationship of the bacillus to the virus is still problematic.

[Thus for instance, in pig influenza it is known that the *haemophilus* bacillus as well as the virus does play an important part in the epidemic. The success of Laidlaw and Andrewes was that they were able to transmit the disease to mice. The fact that one can infect mice by nasal instillation gave facilities for obtaining large amounts of antigen

The type of problems to be tackled come under two headings, first, the performance of routine investigations on patients, such as urea clearance tests, calcium balances and similar procedures, and secondly, and more important, the actual search for new chemical substances in the various secretions of the body. A careful investigation of body fluids will undoubtedly reveal the presence of new substances of the greatest interest both to the chemist from the purely chemical angle and to the biochemist and pathologist.

In the year 1927, for example, the average biochemist would have said that all the urinary constituents were known and that the chemical investigation of this fluid would certainly not lead to any new discoveries. Now we know that up to 1927 enormous quantities of fascinating steroid substances such as œstrone had been steadily poured down the drain in the urine of pregnancy without anyone suspecting their presence. It may well be that as advances are made in the future we shall be still more astonished at what we have been throwing away. It is in this field in particular that we must attract the non-medical chemist and biochemist.

Viruses

By Professor J. McINTOSH

THOUGH never an actual member of the old Pathological Society of London, I have attended some of the meetings in Hanover Square, having been as it were led by the hand by my old chief Professor William Bulloch, so in that respect I may be regarded as a link between the new and the old when such a subject as the theory of the spontaneous generation of life had not died out.

The study of viruses is a relatively new branch of pathology, as the demonstration of the existence of a filter-passing microbe is only some 50 years old, only half the age of this Society, but during the last few years the strides made in the discoveries on viruses and their nature have been enormous, in fact one might almost say that it has become a science of its own.

In the first few years of this century when I was a student, no textbook index included the term "virus" or "virus disease", at any rate certainly not in its present meaning. The discovery of viruses is attributed to Ivanowsky in 1892 who stated that the cause of the disease of plants known as "tobacco mosaic" was due to a filter-passing microbe. His idea was confirmed by Loeffler and Frosch, who transmitted by bacteria-free filtrates the infection of foot and mouth disease, a disease of the utmost importance to cattle breeders in this country and a subject on which much work has since been done.

We now attribute at least 30 diseases of man to viruses—almost as many as those caused by bacteria. The time at my disposal, however, does not allow me to review completely the development of this subject but I would like to deal with the more important discoveries in which members of this Society have played an important part and in which advances were made not only in the technique of approach to the study of virus disease but many new viruses were actually discovered.

The failure to demonstrate viruses morphologically on the ordinary microscope and the failure to grow them on ordinary bacteriological medium gave scope for ingenuity in the development of new processes and procedures for their demonstration, such as in microscopy, centrifugalization, filtration, cultivation in eggs for the discovery of new virus infections.

Microscopy.—The size of viruses necessitated the design of more powerful microscopes.

This was achieved by improving the resolution by the use of ultraviolet rays and special quartz lenses. In this aspect of the work the name of Barnard and his ultraviolet microscope takes a prominent place. Now we have the electron microscope which is capable of almost any degree of magnification and resolution.

The minuteness of viruses had also necessitated a new scale of measurement and for this purpose the micromillimeter or millimicron ($\frac{1}{1000}$ mm.) is used.

Ultra-centrifuge.—For the study of viruses and obtaining large amounts of virus concentrates it soon became apparent that the ordinary bacteriological centrifuge was not capable of providing the gravimetric pull necessary to sediment the virus particles for the purpose of (1) studying the virus concentrates and (2) for the determination of the size of the particles. In this respect one might mention the work carried out by Slesinger at the National Institute for Medical Research and by myself and Selbie at

Section of Ophthalmology

President—P. E. H. ADAMS, F.R.C.S.

[April 11, 1946]

Retinal Periphlebitis.—A. SEYMOUR PHILPS, F.R.C.S.

A. D., aged 42. Lance Corporal.

History.—1945: Vision of the right eye failed partially for a few days and then recovered. He did not see an oculist. No further trouble until March 1946 when the right eye failed suddenly and completely.

On examination.—There is a total R. vitreous hæmorrhage. R. vision is perception of light.

L. eye: Vision 6/9. There are many red cells in the vitreous. On full dilatation of the pupil it is seen that the peripheral retinal veins are thrombosed, and surrounded by hæmorrhage and some exudate. There is also some macular œdema.

The blood in the L. vitreous is increasing slowly, and it seems only a matter of time before this eye also becomes blacked out. The diagnosis seems to be retinal periphlebitis, and he is shown here for the advice of this meeting regarding cause and treatment. All tests have proved negative.

Mr. O. Gayer Morgan said that he had had two similar cases, one that of a man in the R.A.F. who had noticed loss of vision in one eye, for the first time, when he landed in Normandy. When he first saw him in England about a week later one eye was completely destroyed. Presumably there was a large hæmorrhage and detachment. The other eye had a very similar condition to that in Mr. Philps' case—very marked periphlebitis, little hæmorrhages scattered about the fundus, not all peripheral, and it was difficult to tell whether those in the periphery were slightly dilated vessels or small hæmorrhages. The man had gradually settled down with one good eye; he had been on a very light job and was carefully watched. Every single investigation was negative. He first saw the case over a year ago, and the man still had about 6/5 vision in the good eye. The hæmorrhages were smaller, but the periphlebitis was still fairly obvious.

His second case was of a similar type, but this young man was very lethargic, with a "fishy" sort of cold blue hands and cold feet. He had chilblains, and, apparently, his general circulation was poor. Otherwise, again, all investigations were negative. The signs were all in the mid-periphery; there was nothing in the central part of the fundus. One could map out exactly where the changes in the vessels occurred; they were in an area which was mid-peripheral. There had been two hæmorrhages in one eye and three in the other. He carried out a surface diathermy over the area of vascular change, all the way round in both eyes, so that there was a band of grey reaction in the fundus in the area of the change. This was nearly four years ago, and there had been no further hæmorrhage. The treatment did not seem to have affected the eye in any way; there was no alteration whatever in tension.

Mr. E. F. King said that it seemed that these cases were rather more commonly seen in Service patients; he did not know whether that was the experience of others, but certainly he had had several of them in the Army. One case he might mention as an example of what not to do. On the advice of a physician he gave the man dicoumarin, a drug which was cumulative in its effect. There was no result for the first three days, and then the patient had the most violent hæmaturia. It was quite uncontrollable, and only by a series of blood transfusions was the man's life saved. The drug had no effect whatever on the eye condition.

Lieut.-Colonel C. Dee Shapland agreed with Mr. King that this type of case was not unusual in the Army. The condition appeared to be a periphlebitis affecting the smaller retinal veins more especially towards the fundus periphery and associated with multiple thromboses and hæmorrhages. He had had all his cases admitted to hospital and thoroughly investigated but no definite ætiological factor had been discovered. One case was treated with systemic penicillin but without any appreciable effect and others in whom sulphonamides had been employed had also shown no improvement.

Mr. Nigel Cridland said that he had had one case rather similar in type. When he found that the man had a low blood-calcium level he put him on parathyroid and on extra supplies of milk. Whether it was a case of cause and effect he could not say, but there were no further hæmorrhages for five months. He obtained the improvement with doses of parathyroid which kept the blood-calcium level up to about 10.5 mg. per 100 c.c.

Mr. F. R. Neubert said that there were a number of cases in the R.A.F., one of which had been in his hands for quite a time. This man was given tuberculin treatment, and he believed it was seven months since his last hæmorrhage. The patient had asked to be allowed to continue with the treatment because he thought it was doing him good.

The Chairman (Mr. F. A. Williamson-Noble) said that Mr. Philps had been given a variety of suggestions on which he could act. It would be interesting if later he could report what had happened as a result of the method of treatment adopted.

which have been tried out as a preventive vaccine. It is too early yet to make any definite pronouncement on the value of such inoculations.]

Psittacosis.—It had been recorded for some time that the outbreaks of a peculiar type of influenzal-typhoid type of disease was limited to those who had contact with parrots and similar birds of that species. Bedson and Weston in 1930 showed that this infection could be transmitted to budgerigars and mice and demonstrated the presence of virus-like bodies in the infected tissues, thus establishing the virus nature of the disease.

Typhus fever.—With regard to typhus or rickettsial diseases I would like to mention that Professor Matthew Hay, one of my old teachers, was the first to demonstrate clearly that in the outbreak which occurred in Scotland, the disease was spread by lice. A considerable amount of work was done in this country with regard to the relationship of lice to typhus fever and in this respect Bacot and Arkwright in 1923 threw much light on the mechanism by which lice spread the infection. I myself derived intense amusement one evening in watching them perform the tricky operation of infecting lice by rectal injections of *Rickettsia*, a feat of great delicacy—if not of an æsthetic kind.

The virus theory of cancer.—I have left to the last the relationship of the virus to human cancer, because this is still problematic, though many papers have been read in this Section on virus tumours in animals, such as the Rous sarcoma of fowls and the Shope papilloma, by Gye, Andrewes, Peacock, Selbie and myself, particularly on the relationship of carcinogenesis to virus tumours—a problem still not yet completely worked out and which is one of the problems of utmost importance which we have to tackle.

Chemotherapy.—So far chemotherapy has not been so successful against virus infections as against bacterial ones, except perhaps in the case of the *Rickettsial* group. But I might mention that some measure of success has been claimed by Findlay with regard to the use of sulphonamides in lymphogranuloma inguinale and by Bedson with penicillin against psittacosis. That chemotherapeutic remedies are not so successful against viruses is probably due to the differences in the metabolic activities of bacteria and viruses.

CONCLUSION

In conclusion might I say what an amazing new world of the infinitely small has been laid bare in the last half century and I have no hesitation in saying that this period of virus study rivals the golden age of bacteriology of Pasteur and Koch. I am intensely happy to have watched this development and to have taken some part in it and it has given me great pleasure to lay before this Society this review of the last fifty years in which the whole of the energies have been concentrated to the good of mankind and not to his destruction.

Section of Ophthalmology

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OCT.—OPHTH. 1

Bilateral Aphakic Retinal Detachment (A case showing unusual restoration of central vision following reposition).—Lieut.-Colonel C. DEE SHAPLAND, R.A.M.C.

Spr. J. A. A., aged 37, was admitted to the Military Hospital, Shenley, on June 30, 1945. His sight was known to have been defective in both eyes in early childhood, but he was not seen by an ophthalmic surgeon until 1923, when, at the age of 15 years, he came under the care of the late Mr. J. A. Valentine who found lamellar cataract in each eye, the visual acuity of the right eye with -5.0 sph. being $6/9$ and that of the left $6/18$ with -8.50 sph. In 1929 the vision of the right eye with $\frac{-7.5}{-1.0} \downarrow 90^\circ$ had

fallen to $6/12$ and that of the left with -12.0 sph. to $6/36$. Operation was recommended and in that year discission of the left cataract was performed followed six months later by a similar operation on the right, each eye being needled three times. In 1931, the sight of the left eye failed, a retinal detachment was found and was operated upon without success.

In November 1940 the visual acuity of the right eye was $6/60$ unaided, with aphakic correction $6/6$, and that of the left eye no perception of light. Despite this he was called up, went to North Africa in November 1942 and to Italy in October 1943. On April 4, 1945, he walked into a lamp-post in the blackout and sustained a laceration of the right lower eyelid and was admitted to hospital for five days. The ophthalmologist reported—R. aphakia, fundus normal, vision with $+5.0$ sph. = $6/9$. L. tremulous iris, complete detachment with degenerate retina.

On June 18, 1945, J. A. A. noticed a mist over his right eye which rapidly increased and the next day he reported sick. An extensive retinal detachment was found, he was evacuated by air to the U.K. and was first seen by me on July 5. An apparently total detachment of the retina in the right eye was present with a small oval hole supero-nasally some 4 d.d. from the ora, vision being reduced to perception of light only (fig. 1). The case appeared hopeless but the patient agreed to surgical treatment and was operated upon on July 12, 1945—5 surface applications followed by 3 needle punctures over the site of the retinal hole, no muscle being detached. The retina went back and he was discharged from hospital on September 9, 1945, with a full field and the remarkably good central vision of $6/12$ and J. 2 with correction (fig. 2). On April 3, 1946,

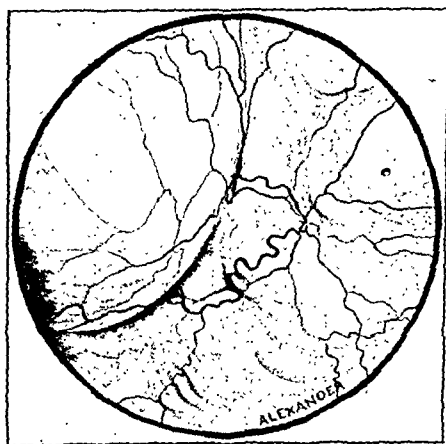


FIG. 1.—Spr. J. A. A. Appearance of right fundus, July 5, 1945. An apparently total detachment of retina with small oval hole at 2.30 o'clock 6 mm. behind ora serrata.

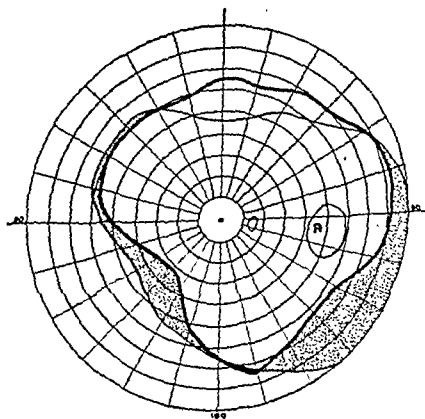


FIG. 2.—Spr. J. A. A. Visual field to $\frac{1}{2}^\circ$ white target September 9, 1945. Central vision with $\frac{+4.0}{+1.5} \downarrow 165^\circ$ = $6/12$ and $+3.5$ added = J. 2.

visual acuity had improved to $6/9$ with aphakic correction $\left(\frac{+4.25}{+1.25} \downarrow 150^\circ \right)$ and with $+3.5$ added he read J. 1 with ease.

This case has been shown as an example of a remarkable restoration of central vision in an apparently total detachment of the retina. The wider question of the advisability of needling of both eyes in cases of congenital cataract is also raised. The incidence of a subsequent retinal detachment following discission of the lens is high. In a paper (1934), I stated that it was probably in the neighbourhood of 10%, and occurred after an average interval of twenty-five years; I suggested that one eye only be needled in childhood, its fellow being left in reserve unless the cataract were so dense as to make

the eye, if unoperated, of little value. In this respect an acuity of 3/60 was suggested as a useful visual standard rather than the 6/18 to 6/24 which had hitherto been fairly generally adopted.

REFERENCE

SHAPLAND, C. DEE (1934) *Trans. Ophthal. Soc. U.K.*, 54, 176.

The Chairman said that the question of needling was constantly arising and it was useful to have the figures given by Colonel Shapland. He recently had a case of this kind, and wished he had known of Colonel Shapland's experience, but he advised that the patient should have only one eye needled. There was the question of amblyopia in the eye which retained the opaque lens. The patient was a child aged 2 years.

Recurrent Proptosis Due to Cavernous Lymphangioma of the Orbit.—EUGENE WOLFF, F.R.C.S.

B. E., female, aged 27.

History.—This case is described in the *Trans. Ophthal. Soc. U.K.* (1932) 52, 298. She has had a number of attacks of recurrent proptosis, the first apparently being at the age of 4 years. The proptosis comes on quite suddenly, the eye being very prominent in a few hours. This is accompanied by a little fever. It takes some six weeks as a rule for it to go back to normal and finally there is some enophthalmos. The disc is now atrophic and there is extensive macular degeneration probably due to interference with the ciliary arteries. She has just had another attack.

The actual diagnosis in this case was made by the removal of a small tumour near the left eyebrow which proved to be a cavernous lymphangioma.

On examination.—All investigations negative. *Treatment.*—Nil significant.

Comment.—Cavernous lymphangioma undergoes recurrent attacks of swelling, most commonly due to inflammation, more rarely to hæmorrhage. Now this swelling is obvious on the surface of the body; in the orbit, however, it manifests itself as a proptosis. Also these attacks of swelling in lymphangioma elsewhere tend to subside spontaneously. In the orbit this would be seen as a disappearance of the proptosis.

Thus, a recurrent attack of inflammation would, in a lymphangioma of the orbit, manifest itself clinically as a recurrent proptosis, and the final fibrosis, no doubt affecting the orbital fat as well, would result in enophthalmos.

Mr. Seymour Philips asked whether Mr. Wolff had had the optic foramen X-rayed.

Mr. Wolff replied that that had not yet been done, but that he would certainly carry out this examination.

Inverse Graphism, Mirror Writing and General Behaviour of Twins.—NOËLLE CHOMÉ, M.B. Lausanne.

Abstract.—Two boys aged 7 years, but mentally aged about 5 years. These children write, draw and read South-North, in other words putting people and letters upside down. One of the twins is often left-handed.

A film taken in the school demonstrating their behaviour was shown.

Mr. Victor Purvis remarked that the two children who were the subjects of this communication would be of interest to physiologists and psychologists for a long time to come. He looked forward to the time—perhaps twenty years hence—when Dr. Chomé would come and tell them the after-history. He gathered that there was a distinction between mirror writing and north-and-south writing. Mirror writing was fairly common. It was found in left-handed children. North-and-south writing and reading characterized few of their patients and he only remembered one case in the out-patients' department where an old lady read for the whole of the morning session, holding the reading matter upside down.

The Optical Control of Sharp Ophthalmic Instruments

By J. F. KAYSER and JOHN FOSTER

INTRODUCTION (J. F.)

SINCE Heinrich Schmidt included in his paper, "Der Einzügige Starschnitt" (*Z.f. Augen.* 1911, 25, 154), a dispassionate estimate of British cataract knives, their reputation has been paramount. Many American oculists used to spend their entire duty-free import allowance on them in prewar days. Of recent years, Swiss knives have gained a good reputation also.

In judging the sharpness of a cataract knife by its operative performance, allowance must be made for variations in scleral toughness, the effects of sterilization, lack of skill in the rapidly changing theatre staff of a training school, and the angle of attack adopted by the operator.

Due allowance having been made for these factors by 1940, one of us (J. F.) had become convinced that the lack of uniformity in performance was due largely to the failure of the trial drum to eliminate defective units. He therefore asked the Master

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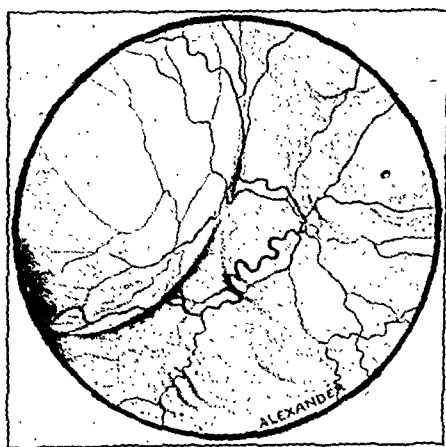


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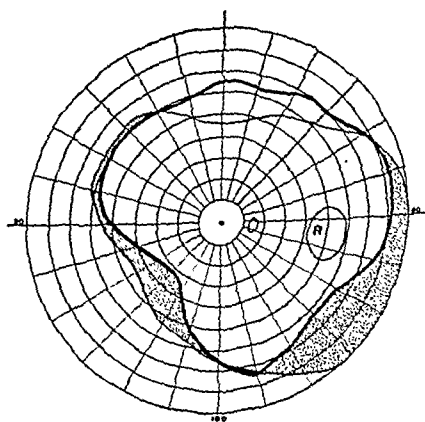


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The relative hardness of a number of cataract knives was found to be as follows:

Weiss A	760
Weiss B	780-810
Grieshaber	730-790

Apart from hardness, blades must possess a certain amount of toughness and this is usually determined by means of an empirical bend test. It is difficult to specify a suitable bend test as it depends so much upon the thickness and shape of the knife.

Beside carbon steels, stainless steel is also used for the production of fine-edged cutting implements. As its name indicates, it possesses the very desirable property of a degree of stainlessness. No steel is, however, absolutely stainless and the term is relative. In spite of possessing a very considerable degree of stainlessness, stainless steel has, however, the disadvantage of requiring a high heat-treatment temperature (approx. 1050° C.), of being insufficiently hard after heat-treatment, and of responding with difficulty to the operations of grinding, honing and stropping. Stainless steel for the manufacture of acute-angled cutting edges should contain not less than 14% chromium and 0.9% carbon.

From time to time cutting instruments have been made from special bronzes, but it is considered that none of them has been sufficiently hard to ensure durability.

Means for measuring sharpness and for determining the exact contour of a sharp cutting edge are available and in constant use.

By the use of specially constructed optical goniometers and of the diamond wedge interference method developed by one of the authors (J. F. K.), the angles of inclination of the minute facets that make up the extreme edge can be measured and the radius of curvature of the edge itself can be determined.

Instruments incorporating light-sensitive cells enable the detection of imperfections that are not visible under the microscope. With a specially adapted profilometer, the depths of grinding marks and of minute scratches on highly polished surfaces can be measured, although the surface itself may be less than 0.001 in. wide. A suitable profilometer is capable of measuring scratches that are not more than 0.000001 in. deep.

It is impossible to produce sharp edges uniformly without means for examining them during production and for that purpose a microscope fitted with a suitable illuminator is absolutely essential.

A standard microscope is quite suitable, but special attention must be paid to the illuminating system. The ordinary vertical illuminator such as is used on metallurgical microscopes is not satisfactory because it may give erroneous results. In this method of illumination a beam of light directed on to the specimen by means of a prism or "cover slip" reflector is reflected back from the specimen into the objective. Unless the surface is flat and at right angles to the optical axis of the microscope, the incident light will be reflected away from the microscope altogether. Since all cutting edges are bevelled, a different system of illumination must therefore be used and experience has shown that the most suitable procedure is to use a dark field illuminator.

The necessity for correct illumination is shown by figs. 2 and 3 which show the point of a keratome photographed at 100 magnifications. Fig. 2 was taken using dark field illumination from a Leitz Ultrapak, whilst fig. 3 shows the same area photographed with an ordinary vertical illuminator. In the second photograph the bevel cannot be seen and an entirely false impression is given of the edge.

Perfect edges are most readily produced by automatic machinery. Some knives, especially ophthalmic knives, unfortunately, do not lend themselves to automatic production. There are several reasons for this. In the first place the knives are very small and are only required in small quantities. Furthermore, the presence of a fixed handle seriously mitigates against automatic production.

All detachable knives should be made by automatic machinery but, unfortunately, some surgeons have a partiality for shapes that cannot properly be automatically produced. The result is that such knives never have a satisfactory cutting edge and, in spite of the fact that the surgeon may be happy with the shape of the blade, it is difficult to see how he can be equally happy with its sharpness. It is suggested that the surgeons should agree amongst themselves what shapes are necessary and, having agreed upon a reasonable number of shapes, should then insist on such knives being properly manufactured. In general, it may be said that straight edges are the most easily manufactured. By the provision of special cams certain types of convex-edged knives can be produced automatically, but there does not appear to be machinery capable of producing knives with concave edges.

As a result of extensive investigations carried out over a number of years, it has been established that the sharpest cutting edges (which unfortunately are only found with any degree of uniformity amongst safety razor blades) are made up of two minute mirror-like facets subtending an angle of 20 degrees to 24 degrees to one another. The radius of

Cutler of Sheffield the best method of testing the sharpness of a knife, and was referred to Mr. J. F. Kayser, the Senior Technician of Gillette Industries Limited.

Mr. Kayser, who is an Associate in Metallurgy of the University of Sheffield, is, I have since learnt, the leading international authority on cutting edges of all kinds, from those used in cutting steel to those used in trimming carpets. He has done much work on the cataract knife problem during the last five years.

PART I (J. F. K.)

A number of factors are involved in the production of sharp, acute-edged cutting implements, and they may be classified as metallurgical or mechanical factors. Metallurgical factors comprise, *inter alia*, choice of material, heat treatment and chemical and physical properties of the heat-treated knife, whilst shape, dimensions of edge, surface finish of facets, &c., are mechanical factors.

Safety razor blades and many surgical knives are made from cold rolled carbon steel containing approximately 1.3% carbon. Cold rolled material containing less than 1.3% carbon may, however, be used and for some purposes it might be preferable to use steel containing not more than 0.7% carbon.

As received from the steel maker, cold rolled steel has a bright, mirror-like surface and every endeavour should be made to preserve this surface throughout the heat-treatment process, and the material should leave the heat-treatment furnace as bright as it entered it. This can be easily achieved if heating takes place in an atmosphere of dry hydrogen or cracked ammonia. Fig. 1 shows two safety razor blade strips; one before heat-treatment and the other after heat-treatment. It will be noted that both look alike.

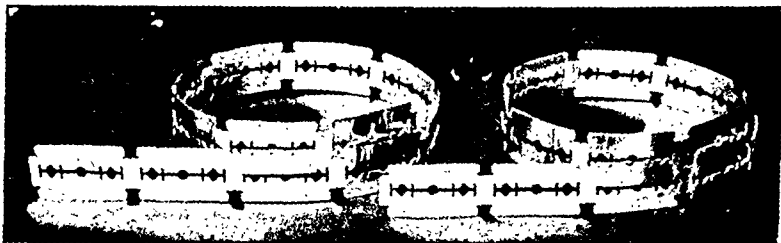


FIG. 1.

In general, the heat-treatment of a safety razor blade or surgical knife comprises two steps, hardening and tempering. Hardening consists in heating to a temperature somewhat above 750°C., the exact temperature depending upon the composition of the steel, and cooling rapidly. Many knives can be heat-treated in strip form and if the cross section is not greater than 0.02 in. it is not necessary to quench in water or oil but one may quench by passing the flat strip between water-cooled blocks. Blades that cannot be hardened between water-cooled blocks must be quenched in oil. Many ophthalmic instruments fall in this latter class.

As originally quenched, carbon steel is too brittle for most purposes and it consequently must be tempered. Tempering consists in heating to a comparatively low temperature (200-400°C.), the exact temperature and duration at the temperature depending upon the type of steel and the physical properties required. This temperature must again be controlled with very nearly the same accuracy as the hardening temperature.

Control of hardening and tempering temperatures is alone not sufficient to ensure a correctly hardened blade, and the product must be sampled and tested for hardness and toughness to ensure that heat-treatment has been satisfactorily carried out.

In the case of very expensive knives heat-treated individually, it is often desirable to measure the hardness of each knife and to submit a small percentage to a toughness test. In the case of blades that may be hardened continuously such as Bard-Parker knives, it is usually sufficient to determine the hardness approximately every 2,000 blades.

There are many different types of hardness tester, adequate descriptions of which are to be found in the technical literature. For such implements as surgical knives, the most useful is the diamond indentation test. In this test a diamond pyramid is pressed into the article to be tested under a constant load, and the hardness number is the quotient of the load in kilograms divided by the superficial area of the impression in square millimetres.

In the hardened state, before tempering, the hardness of acute-angled knives should be not less than 850 and may be as high as 900 to 925. In general, such high hardness goes hand in hand with brittleness and the steel should be tempered to reduce the hardness to approximately 800.

The relative hardness of a number of cataract knives was found to be as follows:

Weiss A	760
Weiss B	780-810
Grieshaber	730-790

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The necessity for correct illumination is shown by figs. 2 and 3 which show the point of a keratome photographed at 100 magnifications. Fig. 2 was taken using dark field illumination from a Leitz Ultrapak, whilst fig. 3 shows the same area photographed with an ordinary vertical illuminator. In the second photograph the bevel cannot be seen and an entirely false impression is given of the edge.

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All detachable knives should be made by automatic machinery but, unfortunately, some surgeons have a partiality for shapes that cannot properly be automatically produced. The result is that such knives never have a satisfactory cutting edge and, in spite of the fact that the surgeon may be happy with the shape of the blade, it is difficult to see how he can be equally happy with its sharpness. It is suggested that the surgeons should agree amongst themselves what shapes are necessary and, having agreed upon a reasonable number of shapes, should then insist on such knives being properly manufactured. In general, it may be said that straight edges are the most easily manufactured. By the provision of special cams certain types of convex-edged knives can be produced automatically, but there does not appear to be machinery capable of producing knives with concave edges.

As a result of extensive investigations carried out over a number of years, it has been established that the sharpest cutting edges (which unfortunately are only found with any degree of uniformity amongst safety razor blades) are made up of two minute mirror-like facets subtending an angle of 20 degrees to 24 degrees to one another. The radius of

curvature of the extreme edge is approximately 0.00001 in. A good edge is never saw-like but is essentially straight even when examined at magnifications as high as 500 times.

A photomicrograph of a sharp cutting edge such as may be found on many safety razor blades and some surgeons' knives made under optical control by modern mass production methods is shown in fig. 4.



FIG. 2. $\times 100$.

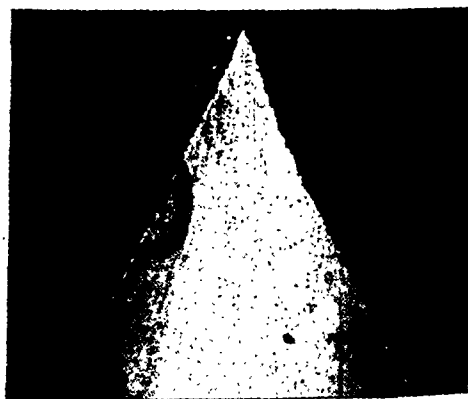


FIG. 3. $\times 100$.

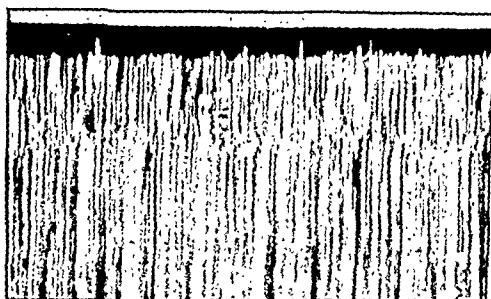


FIG. 4. $\times 50$.

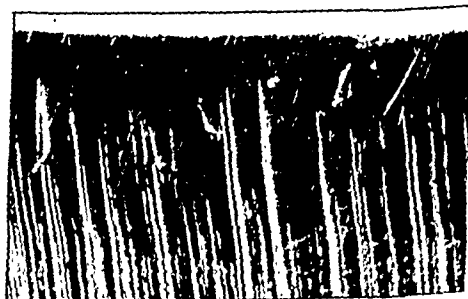


FIG. 5. $\times 50$.

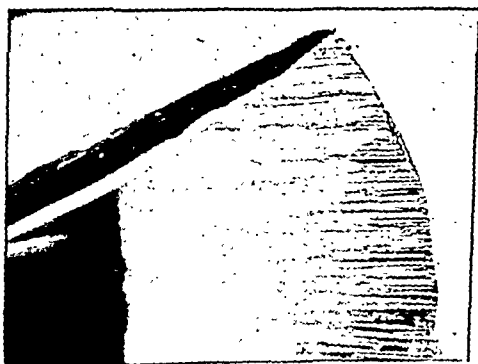


FIG. 6. $\times 50$.

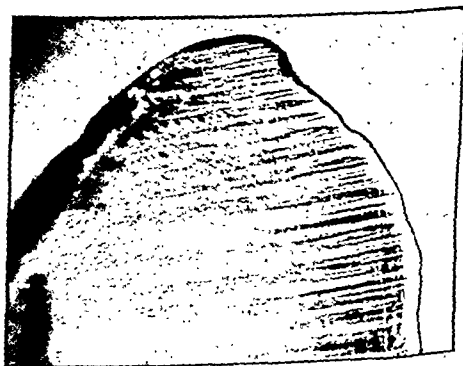


FIG. 7. $\times 50$.

The final facet (the facet adjacent to the edge) is, for all practical purposes, free from scratches, and the few present are less than 0.00001 in. deep.

The final facets of most surgeons' knives appear only to be rough ground, and the scratch depth frequently exceeds 0.0001 in., with the result that the edges are saw-like. Fig. 5 shows the edge of a detachable knife taken from a packet of knives, no two of which were alike and which appeared to have been made without any control.

Figs. 6 and 7 show the points of two knives (both made by the same manufacturer). These were carefully removed from the package by one of the authors (J. F. K.) and the photographs show the blades as they would be received by the operating surgeon. It should be particularly noticed that figs. 4, 5, 6 and 7 were not taken at particularly high magnifications, but only at 50 diameters.

As might be anticipated from their minuteness, sharp cutting edges are extremely fragile and if they are to be packed without damage it is necessary to exercise a considerable amount of thought and skill.

It is indeed highly probable that they undergo more damage when being packaged and at the hands of the theatre nurse responsible for taking them out of the package and sterilizing them than is incurred during normal use.

There are two aspects to the damaging of sharp-edged instruments, namely the mechanical and the chemical side. A slight touch will severely damage an edge and there is a very marked difference in the way in which a really sharp knife and one damaged by careless handling will cut tissue.

Carbon steel cutting edges are particularly prone to corrosion and should always be adequately protected by the manufacturer, but the manufacturer cannot be held responsible for corrosion that may occur when the knives have been removed from the original package.

Particular care must be taken not to damage sharp-edged knives during sterilization. Sterilization of detachable blades at 160°C . for ten minutes is quite permissible as such blades should never be used more than once; repeated sterilization at 160°C . or over will soften the steel.

It must not be forgotten that many sterilizing solutions attack steel.

In general, all solutions having a pH value lower than 7, i.e. possessing some degree of acidity, have a corrosive action on steel. On the other hand, many solutions having a pH value above 7, i.e. possessing some degree of alkalinity, are non-corrosive to steel at room temperatures; at temperatures near to 100°C ., however, some corrosion of the cutting edge may take place and the slightest corrosion is sufficient to blunt a sharp cutting edge.

It is not always possible to predict corrosive tendencies from the presence or absence of a particular element in the sterilizing solution because much depends upon the manner in which the element is combined. For example, free chlorine or iodine, or tincture of iodine, are strongly corrosive to steel, and so also is alkaline hypochlorite. On the other hand, alkaline preparations of chloro-xenols are non-corrosive. A potentially corrosive effect may often be prevented by the presence of an alkaline ingredient. Lysol in alcohol (1 : 2) and liquor chloro-xenolis B.P. both contain soap, whilst liquor boracis et formaldehydi contains borax; all three solutions may be safely used.



FIG. 8.

Care must be taken not to allow instruments to stand in solutions that have a tendency to crystallize out. If that happens small crystals always concentrate on the cutting edge as shown in fig. 8.

Pure alcohol has no corrosive effect on steel but alcohol in contact with air invariably contains traces of oxidation products, i.e. aldehyde and acetic acid, and it then has a tendency to promote corrosion.

curvature of the extreme edge is approximately 0.00001 in. A good edge is never saw-like but is essentially straight even when examined at magnifications as high as 500 times.

A photomicrograph of a sharp cutting edge such as may be found on many safety razor blades and some surgeons' knives made under optical control by modern mass production methods is shown in fig. 4.



FIG. 2. $\times 100$.

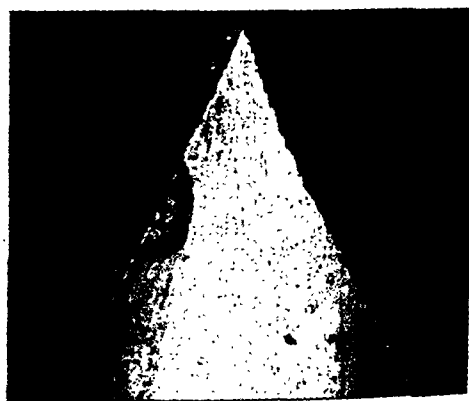


FIG. 3. $\times 100$.



FIG. 4. $\times 50$.

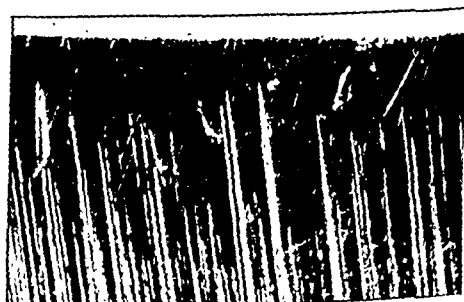


FIG. 5. $\times 50$.

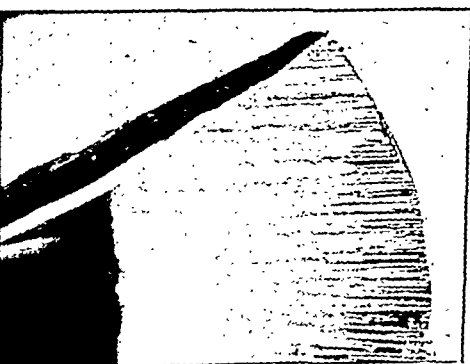


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The Manchester Eye Infirmary is the largest in the country, and has a large stock of new and once used eye instruments ready for use. By permission of Mr. Duthie 122 of these, including cataract knives, needles, keratomes, and trephines, were examined optically (average time per unit 64 sec.).

Group A (unused)

Rejects 11.9% { 2.5% Rust alone
9.3% Constructional defect

Group B (used but still regarded as usable)

Rejects 47% { 11.4% Constructional defect
18.0% Rust alone
17.6% Defect + rust

Are operations easier on the whole with optically selected instruments? After four years of the method my answer is emphatically: Yes.

Can manufacturing methods be improved by optical control? The adoption of a standard (detachable) handle and a uniform size and shape of blade would permit mass production of a knife based on the V. Graefe "Schmalmesser", under optical control with a Gillette edge and a perfect point.

Such a machine is only financially practical if an output of at least 2,000 blades a day could be absorbed.

Hand production requires half an hour's exact and laborious grinding per blade, the final edge being produced by setting up on a hone. The output is limited by the small number of men who can do the work (Downs).

Knives produced experimentally in beryllium bronze and stainless steel were inferior optically and clinically to the usual material (Huntsman's 0.8% carbon yellow label). Points back-sharpened for 2 mm. proved liable to bend.

Trephines.—Experiments are still proceeding to improve the edge by touching with a stone while rotating in an air motor at 20,000 r.p.m. and altering the tempering process to eliminate pits and cracks, though the obturator in a rust-narrowed bore may cause some of the latter.

In conclusion our thanks are due to the Directors of Gillette Industries Limited, Down Brothers Limited, and C. F. Thackray Limited of Leeds, for their help in carrying out this investigation. As lack of space has limited us to a précis of the paper, and a fraction of the large photographic material, it is hoped to republish this paper in *extenso* in the *British Journal of Ophthalmology*.

The Chairman said the authors had opened up all sorts of ideas as to the best way of tackling this problem. He would like to see something in the nature of an N.P.L. certificate issued.

Mr. R. Lindsay-Rea remarked on what he considered to be the value of sharpening the point on the back of the cataract knife. He would not like to use a knife sharpened on the back so much as 2 mm. The first cataract knife he tried was not sharpened on the back. Then it occurred to him that any knife sharpened both back and front must go through best, so he had the back of the knife sharpened 1 mm. He believed it was Mr. A. McCurry who drew his attention to the benefit of that at the time. For a good many years he used that knife, which was manufactured by two firms. In the middle of the war, he supposed, there were difficulties and, for the first time, the point of a cataract knife bent back on him as he was trying to emerge from the anterior chamber. He did not want to withdraw the knife and he could not push it through, so he patiently scratched his way out. He kept the knife carefully and afterwards returned it to the maker, who apologized for a piece of bad tempering. That was the only one out of a great many dozen he had used with which he had had such an accident.

Whatever instrument was devised—a cataract knife had to be good if one was going to get a reliable edge. If one had a good knife it should cut easily through a cornea but one still must saw. He had seen a man take a knife and with one stroke cut through as if cutting through a piece of cheese. It was very severe on the eye, a bad incision; the cut through the cornea did not come back into the sclera. He could not understand his colleagues wanting a whippy knife. The finer the instrument the better, provided it was strong and reliable. His own knife had a strong back and could be trusted; it was possible to cut through without losing aqueous. A number of his knives had found their way across to the United States and there they were being used freely. Some workers had realized that a knife half the size of the Graefe was very effective and a good cataract knife, but it must be well made. The Graefe was too large.

Mr. J. Foster said that he agreed with Mr. Lindsay-Rea that a whippy knife was not good. He had never been able to understand why any surgeon should want a knife of this type, but had been told by the Weiss experts that some surgeons preferred them this way. If any surgeon in the meeting had this preference he would be interested to know the reason for it.

He would like to make clear that the trial drum had never been really adequate for testing trephines or keratomes, and that keratome points were amongst the most defective he examined. As he had explained previously, these instruments were the most difficult of all to make. In addition to this, there were many instruments which would pass the trial drum, but which would not pass the microscope. He had never seen the converse occur.

Stainless steel instruments, as their name implies, are much more resistant to corrosion than carbon steel instruments, but the halogens, e.g. chlorine and iodine, attack them so that even when using stainless steel knives, care must be taken when choosing a sterilizing medium.

PART II (J. F.)

Kayser's methods applied to new and unused cataract knives reveal that a new knife for every operation is no solution of the problem, as about 6 to 10% are defective from rust, have blunt, chisel-like, or oversharpe points, and the edge build-up is inconsistent, sometimes poor, and always inferior to a Gillette blade.

Technique.—To obtain a safe mobility on the moving stage, special holders had to be designed. That illustrated (fig. A) holds cataract knives, needles and straight keratomes, with the ground zone roughly horizontal. Keratomes require a small stand and trephines a device allowing rotation (photographs not reproduced).

Pass standards (knives).—Schmidt's "Einzügige Starschnitt", Terrien's "Mouvements d'Archet", and biopsy of operated cadaveric eyes (St. James's Hospital, Leeds) suggest a

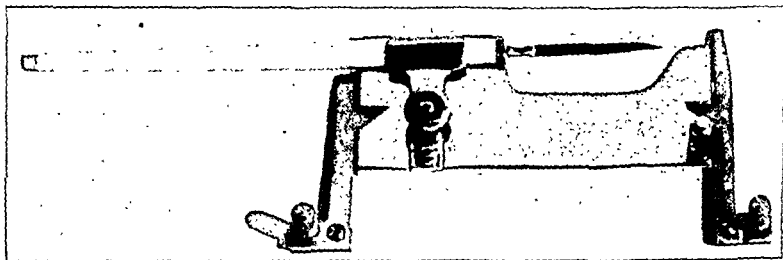


FIG. A.—Cataract knife holder. Lateral notches can be varied to different stage arm fittings.

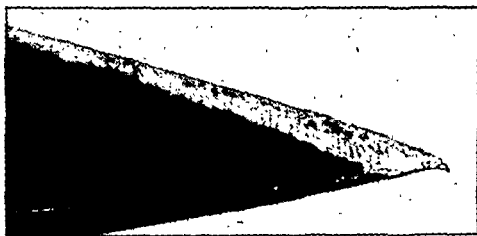


FIG. B.—"Unstable" point. Liable to fracture and remain in the anterior chamber. $\times 240$.

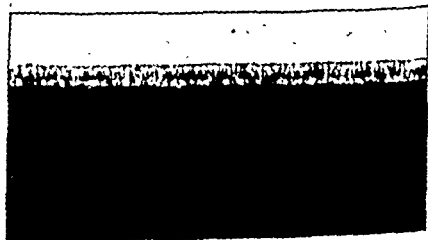


FIG. C.—A good cataract knife edge. Compare the slight irregularity of the edge and the grinding marks with the Gillette blade. $\times 88$.

wedge-cutting action, that a fine point and straight edge are optimal, and that instruments should be used once only.

Surgeons who prefer to "saw", a shortage demanding repeated use, and the limitations of hand grinding, force a compromise on these points.

Exclusion of laterally bent, obviously blunt, and unstable points (fig. B) out of batch of new knives, will leave the rest to provide a rough standard.

A perfect point was shown for comparison (not reproduced) and a photograph of a good edge is seen in fig. C. A slight irregularity is observable. Notches even though < 0.02 mm. wide should reject unless near the heel. Slight rust on the flat can be passed, but not on the ground zone. The best knives have a ground zone 0.03 to 0.07 mm. wide on which the grinding marks are just visible. Ziegler knives have an edge comparable with this when new, and poorer after regrounding. Keratome edges are always inferior to it.

The many British and few Swiss knives examined were superior to most American. Such French and German knives as could be obtained were of a lower standard.

Trephines.—These are softer (VDH 473), and more prone to rust and structural defects (50% in some types) than cataract knives. The problem is which defects can be passed at a time of scarcity. "Chips" out of the ground zone, small notches (unless enlarged by rust) and splits unless curled in or "veed out" can be tolerated though they slow up cutting. In times of plenty such instruments should be rejected and resharpened unless a pitted or perforated barrel indicates future defects. Magnification $\times 40$ is adequate, and the wide objective permits a view of the interior of the barrel.

Are there enough defective instruments in circulation to justify optical control?

The Conduct of a Case Wishing to be Fitted with Contact Lenses

Discussion.—Many patients have quite erroneous ideas as to what can be achieved with contact lenses. After the usual data have been recorded and a short ophthalmic history taken, the purpose for which the lenses are required should be considered. Improved vision not obtainable with spectacles, certain well recognized conditions, such as keratoconus and mustard-gas burns of the cornea, are undoubted indications but most cases do not fall into this therapeutic group. The majority of patients can see well with spectacles but for one reason or another wish to discard them. In that case it is wise to ask: "What do you hope to achieve with contact lenses that you cannot do either with or without your spectacles?" Ball games, swimming, some trade or professional difficulty or disability that can be overcome, are good answers and suggest that the patient is likely to have sufficient drive to master the discipline of contact lens wearing and to use them regularly. It is surprising how many trade and professional difficulties exist which are a great handicap to the patient and which can be removed by contact lenses. Each case should be judged on its merits and candid advice given.

Next the patient should be warned that on the average contact lenses are worn not more than four hours continuously with comfort and efficiency, and it should be pointed out that while he may hope to wear them for more than one such period in one day on occasion he will not be able to do so as a rule. There is a personal limit, varying from case to case, to the hours of continuous wear, the hours of wear on any one day, and the number of hours the lenses can be worn in a week. Four hours a day and twenty-eight hours a week is the average of all cases, both good and bad, in this series. About 20% of cases fall out at this stage.

Fitting of Dixey Lenses

A full routine ophthalmic examination is done. If anything is observed which might make the wearing of contact lenses unwise, such as degenerative changes in the region of the ora serrata, previous needling for congenital cataracts, or any active inflammatory disease, contact lenses should be ordered only after these objections have been carefully assessed for the particular case.

An accurate refraction is now done, the corneal diameters measured with callipers and the patient's corneal radii measured with the keratometer. This use of the keratometer involves complete suppression of the observer's accommodation as is the case in measuring swelling of the optic disc. Absolute readings are required, not the difference which records only the corneal astigmatism. The author uses an Ellis instrument which is robust, very accurate and easily calibrated against a steel ball of known radius.

We may now select from the trial set of afocal lenses a lens of suitable corneal radius and diameter. The scleral radius is estimated by inspection. The lenses in the trial set are all decentred except those in white boxes, and the amount of corneal decentration on each trial lens is the result of experience. It may be altered at will by the prescriber.

Having selected a trial lens it is filled with a solution of fluorescein (1/500 is a suitable strength and is made up in the contact lens solution it is proposed to use).

The lens is now inserted placing the narrow nasal scleral edge towards the patient's nose. The author does not use any anæsthetic drops except in very nervous patients, and it is doubtful if such patients are likely to be successful wearers. If the patient is engaged in conversation and the rationale of each step explained it is unusual to meet any real difficulty. Nevertheless it should be observed that this is the stage at which unpleasant difficulties do arise. If the patient is temperamentally unsuitable, or if his eyes are mixed up in his mind with some psychoneurotic disturbance, he may react violently. This series includes two hysterical fits and one severe fainting attack. Apart from these severe reactions many patients react badly at this stage, becoming pale and sweating profusely. All the severe reactions and most of the less severe ones, have occurred in men. The author does not proceed with such cases, unless the wearing of contact lenses is of real therapeutic importance.

After the lens is inserted it is inspected directly for fit and then examined under a powerful cobalt blue light. This is best obtained by using an ophthalmic operating lamp fitted with a cobalt blue glass filter of suitable density. Plenty of blue light is necessary. Under this illumination the fluorescein fluoresces brilliantly and the very thin film under the lens, wherever it is not actually touching, becomes apparent. This technique of fitting is attributed to Obrig; it is an important advance. While it is best to work with the patient's face turned away from the light, darkness is both unnecessary and undesirable. From this point fitting proceeds by a process of trial and error and is largely a matter of practical experience. It is not proposed to give any detailed instruction but the following diagrams may assist towards an appreciation of the theory underlying contact lens fitting.

[June 27, 1946]

Recent Developments in the Manufacture, Fitting and Prescription of Contact Lenses of Regular Shape

By FREDERICK RIDLEY, F.R.C.S.

THE firm of Zeiss produced spherical contact lenses by grinding in 1892. In 1929 Professor Heine introduced what may be called "the afocal lens approach" and a series of lenses of this type were offered by Zeiss. The range of fittings increased as experience was gained and latterly the full set comprised a range of some 700 lenses.

Even so the necessary range of fittings to accommodate the varying corneal diameter was not provided. It was against this background that Dallos introduced his glass, moulded contact lenses in 1933. These lenses have a scleral segment of irregular contour corresponding precisely to the patient's sclera. This correspondence was at first secured by making the lens to a mould from each eye but latterly has been obtained by adapting by hand a ready-made lens of approximately the correct shape. At one sweep most of the difficulties were removed and a practical contact lens, adaptable to almost any patient that could possibly wear one, became available. The success of the method was so great that the increased cost, the tedious and prolonged fittings by a technician and the troublesome taking of a mould from each eye were accepted and, for the time being, further consideration of the improvements possible along the lines initiated by Zeiss was abandoned.

The introduction of glass-like plastics especially those based upon methyl methacrylate offered a suitable material for contact lenses about 1937 and Obrigg in America succeeded in making a moulded irregular contact lens from this material in 1938. The advantages of this organic plastic are that it is only 40% as heavy as glass and moreover can be used as thin as 0.3 mm. without difficulty; it is unaffected by tears; it is flexible without undergoing permanent distortion and is almost unbreakable; it has a low thermal conductivity so that it feels warm; it has a quality of soft resilience and smoothness when wetted by tears which makes it almost imperceptible to the lids. As developed by I.C.I. in this country, methyl methacrylate, called "Transpex 1", is available with a guaranteed refractive index of extreme precision and its optical qualities are equal and even superior in some respects, to the finest optical glass; it is free from strain and is perfectly homogeneous.

Messrs. Dixey of London attacked the problem of contact lens production from an entirely new angle. They evolved a lathe of such precision that a lens may be turned from the solid block of Transpex. These lenses are not afocal but calculated upon a known base curve for the back surface of the cornea, 7.0, 7.5; 8.0 or 8.5 mm. radius being employed. Experience quickly presented the same difficulties that had formerly confronted Zeiss, but in their new lathe Messrs. Dixey had an instrument of such flexibility that lenses of any corneal or overall diameter: lenses decentred to any amount; lenses made oval to any extent and decentred to any required amount along any axis in relation to the long axis of the oval, were soon produced. The production of a lens correcting astigmatism in both the corneal and scleral portions is also possible.

With such regular lenses consisting of two intersecting curves about three-quarters of the cases suitable for contact lenses can be adequately fitted, the remainder need irregular lenses. The advantages of regular over irregular lenses are ease and quickness of fitting; the fact that a trial of several hours wearing of a lens almost identical with the one it is proposed to order can be made as a routine; the fact that the ordering of a contact lens can be reduced to a prescription similar in form to a spectacle prescription; speed of fabrication (under normal conditions it should be possible to supply a pair of lenses in less than a week), and relatively small total cost. The patient needs to devote normally only one half-day to the fitting and the prescription is handed to him by the oculist as is the case with spectacles. When the lenses are ready he is taught to use them.

The numbers on the drawings define the measurements of lenses and eyes, they will not interest the general reader. The figures for a lens are arranged as follows and are always in millimetres. Scleral radius/ Corneal radius of back surface of lens/ Corneal diameter/ Overall dimensions of lens/ Decentration of corneal part of lens/ The spherical modification of the afocal trial lens used which is needed to give optimum vision/ Vertex distance from front surface of contact lens to centre of principal lens in the trial frame. The last two figures will normally appear only in a prescription. To facilitate inscribing and as a convention, the initial digit and the decimal point may be dropped, thus—12.5 may read 25. The drawings give a true impression of the relationships rather than a diagrammatic one.

FIGS. 1 and 2.—These figures, taken from Obrigg, show the amount of play at the limbus that is desirable in a contact lens. It may be said that no contact lens can be comfortably worn if it presses upon the cornea continuously at any point. Ideally the lens should float symmetrically about the cornea on a tears film which separates it from the sclera, and this relationship should be maintained in all directions of gaze. To meet this requirement when looking nasally as in reading, lenses should usually be decentred.

FIG. 3.—This drawing of two similar circles intersecting demonstrates first, the form of an afocal lens—the shaded area. The surfaces are of similar radius, and are not concentric. Regarded as a lens fitting a globe it is seen that the separation of the two surfaces is greatest at the apex and diminishes to nil in the equatorial region. The width of a 20 mm. lens on a 12 mm. radius scleral circle is drawn to scale and it is seen that the separation at the lens edge is less than one-half of that at the apex. This is important in fitting. A lens of slightly less radius than the eye to be fitted will be supported by a capillary film of tears over a wide area towards the periphery while standing away from the eye centrally. This diminishing separation towards the periphery gives a delicate natural adjustment which the fitter uses to secure his result.

FIG. 4.—Demonstrates the importance of corneal diameter in relation to corneal radius. As the corneal diameter increases the periphery of the corneal segment falls back towards the centre of the eye. Thus, for the same eye, as the corneal diameter of the contact lens is increased the corneal radius may also be increased considerably without touching the cornea. As a corollary we may increase the corneal diameter of the trial lens using the same corneal radius without risk of producing a lens that will touch the cornea. To diminish the corneal diameter without diminishing the corneal radius is to court trouble.

Figs. 5 to 14 are scale drawings to demonstrate the appearance seen when fitting, using fluorescein and blue light, alongside the section of the eye and contact lens.

FIG. 5.—Perfect fitting. Note that a contact lens of corneal radius 8.0 clears a cornea of 7.8 mm. radius if the corneal diameter is 0.3 mm. greater than the actual corneal diameter. This gives the necessary play or lag, see figs. 1 and 2.

FIG. 6.—Too tight, the lens stands away from the eye and rests on its edge where the conjunctival vessels will be compressed and a white area will be seen. The fluorescein fills the lens. Note how much the lens stands away for an error of only 0.5 mm. scleral radius in fitting.

FIG. 7.—Too loose. The lens bears upon the ciliary region and only just clears the cornea. The fluorescein fills the lens at first but is quickly washed away by the tears so that the appearance drawn is more characteristic.

FIG. 10.—If a drop of 1% fluorescein is used the gapping areas will be filled. If the lens is gapping only at certain points, as often happens especially above, the fluorescein will run in as drawn.

FIG. 8.—The contact lens touches the cornea. The fluorescein appearance is of a black central area.

FIG. 12.—These drawings illustrate the two simplest ways in which corneal astigmatism may be accommodated to the sclera. The refraction shows 3 D horizontally which corresponds to corneal radii of 8.0 horiz. and 7.5 vertically approx. Both curves must pass through the same apex. In all three curves the same ideally fitting contact lens is superimposed on the eye. The middle diagram shows the perfect fit in the horizontal meridian. The lower diagram (vertical section) shows the shorter corneal radius carried only as far as the projected scleral curve. Such a cornea would be narrowed in the vertical meridian but the contact lens would fit perfectly. The upper diagram shows the corneal curve carried on to meet the scleral curve at the same corneal diameter (12 mm.) as in the horizontal plane (centre diagram). In this case the contact lens stands away from the eye at the limbus and such a case would probably need a moulded lens.

It may be supposed, however, that the scleral curve in this meridian has to reach the same equatorial diameter as in the horizontal meridian. This means that the scleral radius must be greater in the vertical direction than in the horizontal and the further the contact lens is carried towards the equator the closer it will approximate to coincidence with the sclera. An oval lens with the long axis vertical may fit the eye satisfactorily.

FIG. 9.—Shows, on the left, the wrong way to attempt to fit such a case. The scleral radius of the lens is too small and this produces a tight area horizontally without closing the gap above. The tight area is indicated by strokes and the gapping area, where bubbles will enter in use, is shown by small rings. Diagrams showing the extent of the fluorescein and the tight and loose areas should be made in every case.

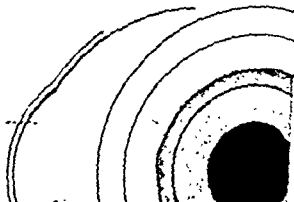
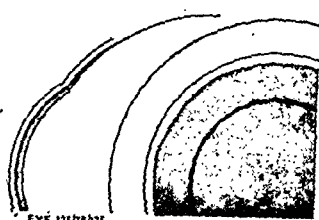
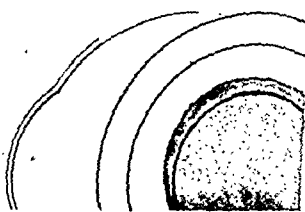
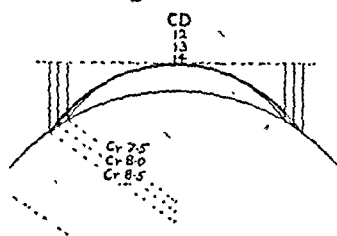
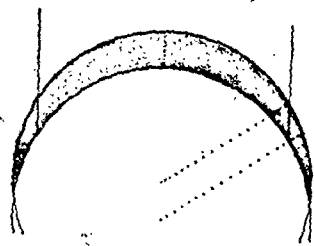
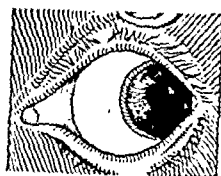
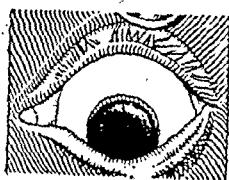
The right-hand picture shows the same case fitted with an oval lens, 19 × 22, of the correct scleral radius. The lens now bridges the gapping area and comes into sufficiently close approximation with the sclera at its upper and lower edges to prevent bubbling.

FIG. 14.—Shows the effect of decentration upon the fit of a lens of slightly shorter scleral radius than the eye. It has the effect of flattening the fit of the narrower flange of the lens.

FIG. 13.—This shows the effect of decentration (drawn upwards for convenience of illustration) upon the fluorescein appearance. Note that the fluorescein pool is concentric with the contact lens flange but displaced in relation to the corneal segment.

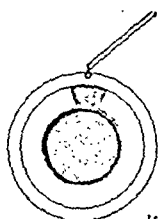
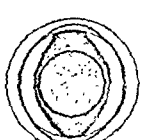
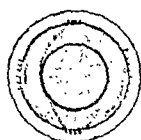
FIG. 11.—To show, left hand, the appearance of a corneal crescent on looking nasally. The lens is pushed against the cornea. This is met by decentring the lens. The centre diagram shows 0.5 mm. decentration which is inadequate, and the right hand diagram 1.0 mm. decentration. This gets rid of the crescent but, as drawn, the lens now fits the sclera right up to the limbus, that is, it is too "flat." The effect on the temporal side is the opposite of that on the nasal side but is of less practical importance.

Acknowledgment is due to T. E. Obrigg for the use of figures 1 and 2 from "Contact Lenses", 1942, New York, and to Dr. P. Hansell, Westminster Hospital Medical School, Department of Medical Photography, for the preparation of the film strip from which illustrations 3 to 14 are taken.

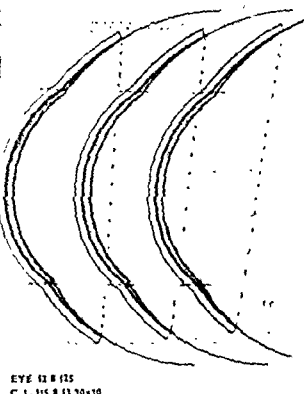
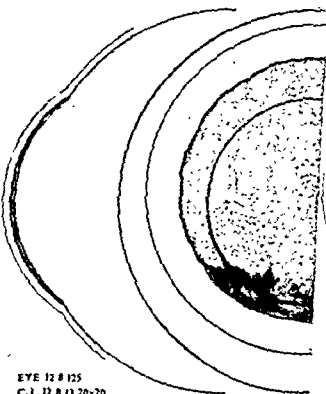
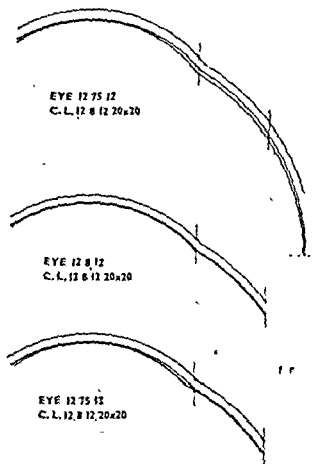


EYE 12 75 12 (D cy 1) \rightarrow
C.L. 12 75 12 20x20

EYE 12 75 12 (D cy 1) \rightarrow
C.L. 12 75 12 20x22



EFFECT OF DECENTRATION ON CORNEAL CRESCENT
AND NASAL AND TEMPORAL FIT



12

13

14

FREDERICK RIDLEY: Recent Developments in the Manufacture, Fitting and Prescription of Contact Lenses of Regular Shape.

Table III shows that after 20% of patients have been rejected at interview, 5% react badly to the fitting (sweating &c.) and 12%, despite a good fit, develop reddening or weeping sufficient to make the ordering of lenses inadvisable. 1% (or rather more) do not tolerate any solution. Of this 18% of "unsuitable" cases some abandon the fitting because, when they have tried the lens in, they decide they do not like the proceeding; no attempt has been made to dissuade such patients. Of the total 65% have been fitted with Dixey lenses and 17% were considered suitable for moulded lenses but not suitable for Dixey lenses.

TABLE III.—ANALYSIS OF 200 CONSECUTIVE CONTACT LENS CASES.
(Rejected as unsuitable at interview, 20%, 40 cases.)

Results (fitting)—160 cases	% of 160 cases
Dixey lenses ordered...	65 or 104 cases
Unsuitable personality	5 or 8 cases
Unsuitable physical reaction to lenses	12 or 19 cases
No solution tolerated	1 or 2 cases
Considered suitable for moulded lenses	17 or 27 cases

Table IV tabulates the answers to a questionnaire sent to all patients in the series resident in the British Isles, many are resident abroad and others were away on service overseas. The answers show that most of the patients are satisfied with their lenses and actually wear them an average of rather more than four hours every day—twenty-eight hours each week. This average includes all those wearing the lenses but excludes those who have given up their lenses for one reason or another (4 cases). 20% wear the lenses less than four hours and must be considered unsatisfactory. On the other hand, 28% wear them more than six hours daily—eight and a half, ten, twelve and thirteen hours daily average occur in the 29 replies received and this figure is perhaps unexpectedly good

TABLE IV.—RESULTS IN USE.

A questionnaire was sent to the 60 patients living in Britain and 29 replies received.

<i>Are you satisfied with your lenses?</i>			
Yes	20	70%	
No or qualified Yes	9	30%	
Cannot put them in or "lost interest"	4	13%	} 30%
Worn two hours or less	5	17%	
<i>How long can you wear them?</i>			
Average of 19 replies giving actual figures	5½ hours		
<i>How long do you wear them?</i>			
Daily average (29 replies) excluding 4 not wearing	Hours		
5	2	20%	
8	4	32%	
5	4-6	20%	
7	Over 6	28%	
Average of exact times given	4½ hours.		
<i>Weekly average</i>			
Average of exact times given	28 hours.		

Apart from the questionnaire the records contain 49 reports of times worn—by patients or friends reporting about them. The average is again five hours, which suggests that the above detailed analysis may be reasonably regarded as a fair sample of the whole series.

CONCLUSION

This review of the case history of 200 consecutive patients who sought to wear contact lenses is perhaps the first of its kind. Similar analyses of larger numbers by different workers will be needed before any definite conclusions as to the efficacy of contact lenses as a whole, or of any particular type, can be arrived at. It is believed that this series justifies a revival of interest in the spherical or regular type of lens. The series suggests that some 80% of cases suitable for contact lenses can be fitted by the Dixey pattern lens leaving not more than 20% needing the irregular type, usually made to correspond to a mould taken from the eye. Probably all cases should be tried with the Dixey pattern lens in the first instance in order to eliminate those who prove unsuitable for personal or physical reasons.

An important aspect of this problem is the fact that Dixey lenses are ordered on a prescription similar to that normally employed for spectacles. In suitable cases the surgeon can conduct the whole examination and fitting in half a day in his consulting room, arriving at a clear formula to which the lenses can be made with great accuracy and in a short time. By this means a patient can visit any surgeon with the necessary training and obtain his prescription in a few hours. Unsuitable cases are eliminated quickly and with the minimum of trouble and expense to the patient. Moreover the decision as to whether a patient is suitable or not rests, as it is submitted it should do, with the surgeon. Many factors have to be assessed which belong properly to the sphere of the oculist and not to that of the technician. The fitting itself demands accuracy of

The fitting completed, the refraction is done again to determine the modification necessary. There is a tendency to accommodate strongly for some time after the lenses are fitted and this must be looked for. The following rules are of general application.

(1) The additional lens will be very near indeed to the addition predicted by the Zeiss charts if the first refraction, the keratometer readings and the fit are correct. A discrepancy of more than 5.0-5 should excite suspicion that something is wrong.

(2) The two eyes will show almost exactly the same deviation from the predicted values and in the same sense unless there is considerable anisometropia.

(3) The refraction with the lens in should be done with cylinders exactly as is the practice for spectacles. Some lenticular astigmatism is commonly found and the spherical modification of the lens ordered should be the sphere of the full correction excluding the cylinder. If this is not done, either axis of the total refraction may be corrected, perhaps in the opposite sense in the two eyes. This produces accommodative imbalance and difficulty with contact lenses just as it does in wearing spectacles. Some visual acuity must be sacrificed but the cyl. involved rarely exceeds 0.75.

Typical Prescription

			Date	
R.E.	Ref'n: S. -2.75/-0.75 @ 120°	6/5	L.E.	Ref'n: S. -3.50/-0.5 @ 60°	6/5
	C.L.: 25/8/13/20 × 22			C.L.: 225/8/13/20 × 22	
	dec. 0.5 mm. L.A. (long axis)			dec. 0.5 mm. L.A.	
	Add minus S.3.5			Add minus S.4.25	
	at 9 mm. V.D.	6/5		at 9 mm. V.D.	6/5

It has been observed repeatedly in eyes showing no astigmatism by retinoscopy or subjectively, that the keratometer shows up to 0.75 of corneal astigmatism compensated by the same amount of lenticular astigmatism, as shown by the final refraction with contact lens in. The mechanism of this is not clear. It would appear that corneal astigmatism may be compensated to a limited degree by an opposite lenticular astigmatism possibly due to unequal ciliary contraction. The alternative would be that the cornea or the lens grows so as to produce a compensating astigmatism.

TABLE I.—PERCENTAGE ANALYSIS OF 200 CONSECUTIVE CONTACT LENS CASES.

				200 cases				
Sex:	Males	63	Refraction:	Over plus 5	...	1
	Females	37		0-plus 5	...	6
						0-minus 5	...	60
Age:	20 and under	8		- 5 to -10	...	18
	20-30	65		-10 to -15	...	15
	30-40	20		-15 to -20	...	0
	40-50	7	Astigmatism of 2 to 3 D	4
Purpose:	Sports	35		over 3 D	...	3
	Trade and profession	29	Result of interview—			
	Social	32		Considered suitable for C.L.	...	80
	Special	4		Considered unsuitable	...	20

Table I shows a big preponderance of males, perhaps due to the large number of Service men seeking lenses in the latter part of the war period. The 20 to 30 age-group is much the largest. The cases are evenly distributed between those seeking lenses for sports, trade and professional, and social reasons. Myopes of low degree dominate the picture.

TABLE II.—ANALYSIS OF 200 CONSECUTIVE CONTACT LENS CASES.

Contact Lens Measurements ordered	%	second	
	100*		
Scleral radius:	11.5 mm. or less	...	0
	11.75 and 12.0	...	23
	12.25	...	45
	12.75	...	32
	over 13.0	...	0
Corneal radius:	7.5 mm.	...	6
	8.0	...	65
	8.5	...	29
Corneal diameter:	12.0 mm. or less	...	4
	12.25 and 12.5	...	12
	12.75	...	33
	13.0	...	43
	13.25	...	12
	13.75	...	0
	over 14.0	...	0

* A wider range of trial lenses became available for the second hundred cases.

Table II shows the distribution of contact lens measurements. The majority of scleras have a radius of 12.5 mm. The corneal diameter is at least 13 mm. on the average.

Further detailed analysis shows that there is no correlation whatever between the scleral and corneal measurements. Thus in the whole series there are very few cases of "average" eyes (i.e. 12.5/8/13) while 11.5/8/14 and 13/7.5/12 actually occur. These findings suggest that these measurements are biologically independent of one another.

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refraction and a good deal of judgment which surgeons already possess by reason of their training and experience.

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Professor Ida Mann said that Mr. Ridley had given a most interesting account of a group of cases of which she had no real experience. Her own cases had not been comparable, in that she had omitted the cosmetic group and had dealt almost entirely with patients showing an absolute rather than a relative indication. She had found that the Zeiss type of lens gave often good results in conical cornea, but not usually in the other groups. She had had one or two interesting cases which had started with Zeiss lenses, but had been dissatisfied with the short length of wear—four hours—and had demanded a longer wear and this had been obtained with individually fitted lenses. She had encountered now and then an hysterical case, and her experience was that one should not despair even of hysterical people; she had urged them to go through with the individual fitting, and some of them had acquired complete tolerance. Many of her patients were unable to work without contact lenses and therefore required a minimum tolerance of eight hours a day. In one series of 84 such cases this had been attained in 39 of them with individually fitted lenses.

Mr. Purvis asked whether the new plastic material used was any harder than the material in current use for spectacle lenses.

The Chairman (Mr. Humphrey Neame) said that his experience as to the length of time such lenses could be worn had been that different cases varied considerably. He had had mostly to deal with mustard-gas keratitis pensioners. The people concerned wanted to use their lenses for as long as possible so as to do a day's work. Some of them wanted to use them for twelve hours a day. He had not got all the figures but certain of these keratitis cases did not tolerate the lenses for more than three or four hours, while a good proportion of them were able to wear them for eight to twelve hours.

Mr. Ridley, in reply, pointed out that the minute "scratches" which occur on most plastic lenses after they have been in use for some time, are not true scratches but rather what are technically called "sleeks". The material is not fractured at the edge of the mark but there is a faint depression with rounded, often slightly raised, edges. Such marks are obliterated by the tears film. True scratches involving loss of material are caused by quite gross damage and do not occur with reasonable care in use.

With regard to hysterical cases, unless there was a strong therapeutic indication, he did not try to overcome a serious hysterical disability. Very few patients would tolerate anything in actual contact with the cornea. There was, however, a much greater range of corneal sensitiveness than was usually supposed even among normal patients.

Miliary Aneurysms in the Macular Region of the Left Eye.—P. MCG. MOFFATT, F.R.C.S.
 L. W. J., male, aged 37.

History.—Ten years ago he had pulmonary tuberculosis which was treated by pneumothorax. Dr. Andrew Morland reports that he has had no sign or symptom of active disease for at least eight years. The left lung shows much fibrosis, but is unlikely to be causing toxæmia.

In 1943 he consulted me on account of headaches and pain in the eyes on close work. There was considerable hypermetropic astigmatism which was undercorrected, and deficiency of convergence. No abnormality of the fundi was noted. New glasses and a course of orthoptic exercises relieved the symptoms. Early 1946 he complained of frontal headache and aching of the left eye. R. and L. vision with glasses = 6/5, and Jaeger 1. Convergence good, fundi appeared normal. Orthoptic exercises did not help. There was congenital absence of the left frontal sinus but no signs of infection. In April the vision was 6/5 in each eye with glasses, but minute swellings were noted on the vessels surrounding the macula of the left eye.

On examination (20.6.46).—Complains of a sense of strain after reading for a short time. R. and L. vision with glasses 6/5, and J. 1. Convergence good. The right fundus appears normal, the left fundus shows several very small saccular dilatations on the arterial twigs surrounding the macula. These appear to have increased in number in the past six weeks. Urine: Normal. W.R. and Kahn negative.

The Chairman recalled a case of his own—a man, aged 29, whom he saw about twenty years ago, who had discovered that his vision in one eye was affected. He had some aneurysms, larger than in the case now shown, the largest being about three times the diameter of a main retinal artery, and the smaller ones were perhaps of equal diameter to that artery. They extended over a considerable area of the macula, and the vision was quite markedly affected. The patient only discovered his condition while driving a cart. His and, getting some dust in his good eye, found that he could not see with the other. His condition remained very much the same for a number of years. He had now a more complete central scotoma, with a good deal of diffuse exudate in and around the macula. The case now shown might represent a much earlier or more elementary stage of a similar condition. It would be interesting to see his condition in ten years' time.

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